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A Case Report of Idiopathic Hypogonadotropic Hypogonadism

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Abstract

We describe a case of a 21-year-old male with absent secondary sexual characters, and erectile dysfunction since puberty. The clue to his underlying disorder came with a hormonal assay, which was suggestive of secondary hypogonadism. Futher workup, was done to detect other causes of hypogonadism, which was normal, hence we concluded the patient to have Idiopathic hypogonadotropic hypogonadism. This is an uncommon cause for hypogonadism and infertility and represents one of the few treatable forms of hypogonadism.

Key words: GnRH deficiency, hypogonadism, testosterone replacement

Introduction:

Idiopathic hypogonadotropic hypogonadism (IHH) is a selective failure of neuroendocrine components of the reproductive system in the absence of an anatomic or functional cause[1]. There is a deficient secretion of hypothalamic gonadotropic releasing hormone (GnRH) that in turn is responsible for abnormal gonadtropic secretion, resulting in hypogonadism, infertility, absent, incomplete or partial pubertal maturation. The clinical presentation of IHH is similar to Kallmann syndrome, except in latter have features of anosmia or severe hyposmia. IHH is sporadic or familial in occurrence, with the latter inherited in either X-linked or autosomal mode [2] and with a prevalence rate 1 in 10,000 population[3]. We describe a case of a 21 year old male presenting with absent secondary sexual characters and erectile dysfunction. On clinical examination, hormonal assay and imaging studies, patient had secondary hypogonadism .In the absence of systemic disorders, other endocrine abnormalities and intracranial lesions, he was diagnosed to have IHH .We would like to report this case, since it is a rare disorder and it is usually less recognized in clinical practice.

Case history:

A 21-year-old male presented with undeveloped facial, axillary and pubic hair, lethargy and erectile dysfunction. Patient did not have any co-morbid illness in the past. Patient had attained normal milestones until puberty with an average academic performance and he had discontinued his studies from the age of 17. He was investigated in a hospital near his hometown in 2002 and those reports showed thyroid stimulating hormone (TSH) levels of 2.8mIU/ml, testosterone of 0.1 ng/ml, luteinizing

hormone of 0.09mIU/ml .He was given human chorionic gonadotrophin injections, but discontinued it due to monetary constraints.

On examination, his weight: 45 kg, height: 161cm, arm span: 164 cm upper segment: 71 cm lower segment: 90 cm (ratio - 0.78) .He had low-pitched voice, absence of facial, body, axillary and pubic hairs. Examination genitals showed a small penis (6 cm), absence of scrotal pigmentation and both testes were palpable in scrotal sac. Patient's olfactory sensation was intact, which was tested using aromatic substances like coffee and perfume. There was no other clinical abnormality. Ophthalmic examination showed a normal fundus with no visual field defects.

On admission to our hospital, hematological and biochemical investigations, including serum ferritin were within normal limits. The serum luteinizing hormone (0.1 mIU/ml), follicle-Stimulating hormone (0.2 mIU/ml), testosterone (0.02ng/ml), levels were low. Serum prolactin (11.2 ng/ml), T3 (0.9), T4 (5.1), TSH (3.2) levels were within normal limits. Ultrasound abdomen was normal, ultrasound of scrotum showed bilateral small testis, and epidydimis.CT scan head with coronal cuts was essentially normal. Karotyping of the blood showed 46XY pattern. Patient was initiated on testosterone depot 100 mg intramuscularly once in 3weeks and the dose and frequency was increased to 250 mg once in two week subsequently.

Discussion:

Idiopathic hypogonadotropic hypogonadism is an endocrine abnormality due to isolated gonadotropic releasing hormone deficiency, presenting with absence of pubertal development and respond to treatment with exogenous, pulsatile GnRH, thus localizing their defect to the hypothalamus rather than the pituitary. This disorder is common in males (males to female ratio ranges from 4-5:1) and with a frequency of one in10, 000 population[3.] Family members of patients with IHH may have history of delayed puberty compared to the general population[2]. The genetic basis for idiopathic hypogonadotropic hypogonadism is largely unknown; mutations in several genes involved in the hypothalamo-pituitary-gonadal axis development and function have recently been implicated in the pathogenesis of this condition (DAX-1,X–linked)[4].

Patients with IHH may not experience puberty or may experience incomplete puberty with symptoms of hypogonadism. In men, symptoms include absence of axillary, body and pubic hair, decreased libido, erectile dysfunction, decreased muscle strength, and diminished aggressiveness and drive. Women, present with symptoms of amenorrhea (primary), dyspareunia and infertility[5]. In adults, there is increased risk of fracture due to osteoporosis[6] .On physical examination patients have eunuchoidal skeletal proportion, upper body segment to lower body segment of less than 1:1 and

arm span length to height of more than 5 cm; where as the height for age may be normal. Along with the features of hypogonadism, males have small penis (<8cm), loss of scrotal pigmentation and cryporchidism in small percentage of patients. Females encompass lack of breast development and failure of squmaous epithelial differentiation of the vaginal mucosa. The clinical presentation of IHH is similar to Kallmann syndrome except for absence of anosmia or severe hyposmia.

Laboratory examination should aim at identifying the causes of hypogonadism, which could be due to systemic diseases, other endocrine abnormalities or intracranial lesions like craniopharyngioma. Serum luteinizing hormone, follicle-stimulating hormone and serum (total or free) testosterone (in males) /estradiol levels (in females) are low. Screening for serum prolactin, TSH and ferrtin (for hemochromatosis)[7] is important and will be essentially normal. Imaging studies especially of the brain is essential to rule out intracranial lesion of the pituitary and hypothalamus [8].

Gonadal steroid replacement therapy can reverse the hypogonadism and restore fertility. Androgen replacement in males restores libido, erectile function, and well-being and promotes the development of secondary sexual characteristics[9]. Androgen replacement also improves bone density and may prevent osteoporosis. Testosterone is the drug of choice for androgen replacement and is administered as injections at the dose of 100 per week or 200-300 mgs IM once in 2-3 weeks (Testosterone Enanthate /Cypionate as esterified oil-soluble preparation) [10] .

In our case patient presented in the adult stage with features of hypogonadism and on investigating had feature of secondary hypogonadism, with no other systemic, endocrine causes and in absence of intracranial lesions, we concluded the disorder as IHH. The patient is on testosterone depot injections and is he tolerating the treatment well.

An early recognition of hypogonadism and investigating for the cause is important. Although the causes of IHH are unclear, its timely diagnosis and treatment is vital, since it represents one of the few treatable forms of hypogonadism.

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