

Idiopathic Hypogonadotrophic Hypogonadism (IHH) with Pickwickian Syndrome, Cor Pulmonale and Insulin Resistance.

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Abstract: Idiopathic hypogonadotrophic hypogonadism (IHH) is a congenital/ developmental defect of the hypothalamus leading to deficient GnRH and resultant hypogonadism. Serum levels of FSH, LH and testosterone in males are decreased. Obesity is a rare association. We present a case of a 25 year old male with IHH, obesity- hypoventilation syndrome with cor pulmonale, diabetes mellitus and hypertension.

INTRODUCTION

The aetiology of hypogonadotrophic hypogonadism (IHH) depends on various conditions. It may be caused by a selective gonadotropin deficiency or by concomitant lack of other pituitary hormones in the context of a more complex pathology. It could be congenital or late onset in the adult male, because of a known condition. The location of the damage could be at the hypophyseal or the hypothalamic level. Congenital hypogonadism presents isolated gonadotropin deficiency with anosmia or hyposmia mostly caused by a genetic abnormality associated with the KAL1 gene and is also known as Kallman Syndrome. IHH is similar with Kallman Syndrome but without anosmia or hyposmia. The acquired forms present multiple alterations of the hypophyseal function and are brought on by conditions such as inflammatory diseases, hypothalamus- pituitary expansive pathologies (adenomas), immune disorders. Chronic diseases, some psychiatric illnesses, important nutritional disorders, such as anorexia nervosa, could also determine a gonadal dysfunction.

CASE REPORT

A 25 years old obese male was admitted to our ICU with history of swelling of both lower limbs since 20 days and episodes of drowsiness, difficulty in breathing since 10 days. On examination he was obese (BMI-36.6, fig 1), pulse was 70/min, RR- 10 breaths/min, BP- 138/86 mm of Hg, pallor, cyanosis were absent. JVP could not be accessed because of obesity. There was bilateral pitting edema of feet. Further examinations revealed, acanthosis nigricans, absent secondary sexual characteristics (fig2), micropenis (fig 3), small testes, underdeveloped scrotal sacs with loss of scrotal rugosity. Leading questions revealed hyperphagia, weight gain since childhood. There was no history of headache, diplopia, visual problems and seizures.

Cardiovascular system examination revealed distant heart sounds, Respiratory system examination revealed bradypnea and bilateral diminished air entry. Abdomen examination revealed soft, tender hepatomegaly of 4 cms below right costal margin. On CNS examination, patient was drowsy and responding to questions intermittently, flapping tremors were present, cranial nerves normal, mild hypotonia was present in all four limbs, DTR present, Plantars were bilateral flexors. Sensory system was normal.

Investigations: Hb – 11.2 gm/dl, TLC, DLC, KFT, LFT were normal, urine-normal, serum electrolyte studies were normal, FBS- 360 mg% , Post prandial blood sugar 442 mg%, Fasting lipid profile normal, ECG showed low voltage complexes, ABG- PH=7.30, PaO₂=55mm of Hg, PCO₂= 66mm of Hg, SaO₂=88%, HCO₃=34mm of Hg, D (A-a)O₂ normal, suggestive of chronic respiratory acidosis due to pure alveolar hypoventilation. Further ABG reports repeatedly demonstrated resting hypoxia, hypercapnia which especially increased during sleep. CXR normal. PFT showed restrictive pattern. 2D Echo revealed dilated right heart with moderate pulmonary hypertension. CT brain with contrast- normal study, USG scrotum- revealed bilateral small sized testis ,(right testis 1.6*1.1cm, left testis 1.1*1.1cm). EEG – normal study, Serum FSH - < 0.30 mIU/l (1.4-18.1), Serum LH - < 0.07 mIU/l (1.5- 9.3) , Serum Testosterone – 6.43 ng/dl (280- 800), Serum PRL – 2.33, Serum TSH – 3.09, Serum ferritin normal. Fundus examination was normal. Perimetry did not reveal any hemianopia. MRI pituitary

showed mild hypoplasia of anterior pituitary.(Fig 4) A diagnosis of Idiopathic Hypogonadotrophic Hypogonadism (IHH) with Obesity Hypoventilation Syndrome and Cor Pulmonale was entertained.

He was treated with Volume cycled NIPPV for the respiratory problem. Diabetes was controlled with Insulin and metformin. CCF was treated with diuretics and ACE inhibitors. ABG improved. Injection Testosterone enanthate 100 mg IM was given to be repeated every 1 month. He declined GnRH therapy due to monetary constraints. Patient took discharge on request.



Fig 1: Showing Obesity



Fig 2: Showing Acanthosis Nigricans



Fig 3: Showing Micropenis and underdeveloped scrotal sac

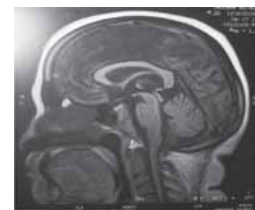


Fig 4: MRI of brain showing hypoplasia of anterior pituitary gland.

DISCUSSION

Male hypogonadotrophic hypogonadism encompasses the pathology involving the hypothalamus and/or pituitary. Infections, infiltrations, radiation therapy are the common etiologies associated with panhypopituitarism. Some of the developmental or congenital conditions include pituitary aplasia or hypoplasia. Commonest Hypothalamic GnRH deficiency disorder is known as Kallman Syndrome when IHH is associated with anosmia or hyposmia. The gene responsible is KAL-1¹. When anosmia or hyposmia are not documented, then the diagnosis of IHH is made. Idiopathic hypogonadotrophic hypogonadism (IHH) is a selective failure of neuroendocrine components of the reproductive system in the absence of an anatomic or functional cause. IHH is sporadic or familial in occurrence, with the latter inherited in either X-linked or autosomal mode and with a prevalence rate 1 in 10,000 population^{2,3}. This disorder is common in males (males to female ratio ranges from 4-5:1) and with a frequency of one in 10,000 population.

The genetic basis for idiopathic hypogonadotrophic hypogonadism is largely unknown; mutations in several genes involved in the hypothalamo-pituitary-gonadal axis development and function have been implicated. The most common genetic defect lies in the DAX 1 gene and the mode of inheritance is X-linked⁴. Patients with IHH may not experience puberty or may experience incomplete puberty with symptoms of hypogonadism.

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