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RESEARCH ARTICLE

A CLINICAL CASE OF A PRIMARY PARTIAL EMPTY SELLA PRESENTING WITH HYPOGONADOTROPIC HYPOGONADISM

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Abstract

Primary empty sella (PES) is a rare condition characterized by the herniation of the subarachnoid space into the sellaturcica, with variable filling of cerebrospinal fluid (CSF). We present a clinical case of a 19-year-old male with primary partial empty sella who presented with hypogonadotropic hypogonadism, a condition typically observed in females at an older age. The patient exhibited delayed puberty with characteristic hormonal abnormalities and bilateral atrophic testicles. Magnetic resonance imaging (MRI) revealed a partial empty sella with preserved pituitary function. Hormonal replacement therapy was initiated, leading to improved virilization; however, fertility induction was unsuccessful despite intervention. The etiology of PES remains unclear, with proposed mechanisms involving sellar and pituitary factors. Genetic studies have identified candidate genes associated with PES development. Hormonal replacement therapy remains the cornerstone of treatment, aiming to alleviate symptoms and prevent long-term complications. This case underscores the importance of early recognition and management of hypogonadotropic hypogonadism in male patients with PES, with consideration for comprehensive therapeutic approaches, including fertility induction where appropriate.

Introduction:-

Empty sella or "arachnoidocele" is characterized by the protrusion of the subarachnoid space into the sellaturcica, which can be occupied either entirely (>50%) or partially (<50%) by cerebrospinal fluid (CSF)[1]. Primary or secondary empty sellacan be distinguished based on the etiology. The pathophysiology of primary empty sella (PES) is unknown, in contrast to secondary empty sella, which is brought on by pituitary pathological circumstances such as prior surgical, pharmaceutical, or radiation treatment [2].Among the mechanisms that have been found are the involvement of suprasellar or pituitary stimulating factors, as well as insufficient creation of the sellar diaphragm [1].Its incidence is not very high, ranging from 8%–35% in clinical practice to 5.5%–12% as an inadvertent finding in autopsy. The majority of PES cases occur in women, specifically in those with a physiological history of at least one successfully completed pregnancy. It also occurs less frequently in children than in adults, and it is generally linked to prenatal complications, genetic diseases, and hypothalamic-pituitary dysfunction [2]. Here we emphasize a case of a PES in a male patient with no medical record linked to this condition.

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Clinical case

A 19-year-old male patient was admitted to our department for delayed puberty. He was born full-term via normal vaginal delivery, with no perinatal complications. The patient has good psychomotor development, and no medical record. Physical examination found a height of 1.24 m, data such as the weight has been lost. He has no genital or pubic hair development (graded as Tanner Stage 1). He has a stretched penile length of 3 cm (which falls more than 2.5 standard deviations below the mean for the age), and the testicular volume was 3 ml.The hormonal assessment showed hypogonadotropic hypogonadism and no other pituitary insufficiency. The patient had a normal karyotype; however, there is no information available regarding his bone age. Testicular ultrasound revealed bilateral atrophic testicles. The CT scan of the brain showed no abnormalities, while the MRI revealed a partial empty sella with preservation of the normal hypersignal of the post-pituitary gland, a thin median pituitary stalk, and intact olfactory bulbs. The patient was diagnosed with Primary Empty Sella (PES) (Partial) based on the MRI findings, resulting in prepubertal hypogonadotropic hypogonadism. He was offered testosterone therapy for puberty induction.

Table 1:- Hormonal profile of present case.

Test	result	Normal value
FSH	0.36	1-12 mUI/ml
LH	0.12	0.5-5.8 mUI/ml
Testosterone	0.8	4.5-42 ng/ml
Prolactin	7.2	5-15 µg/l
Cortisol	17.05	6.2 - 19.4µg/dl

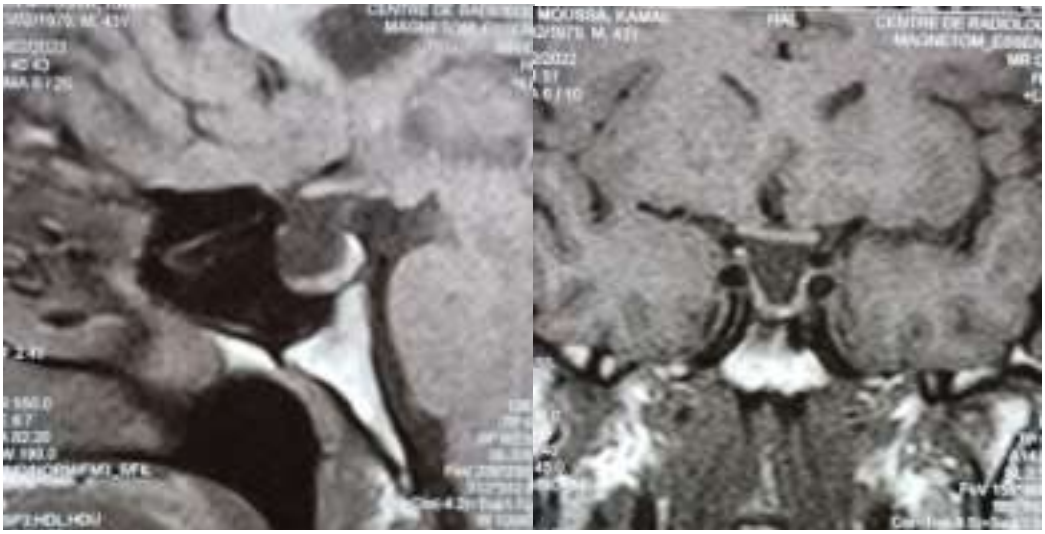

Figure 1:- MRI images showing a partial empty sella with a laminated pituitary gland.

At the age of 41, which is 6 years after his marriage, the patient consulted for a second time due to fertility problems (while noting that his wife had been on oral contraception throughout this period and stopped because she wanted to conceive). The assessment of the wife showed no abnormalities. The patient has been taking testosterone for 22 years, using it regularly. He reported experiencing libido and spontaneous erections. His clinical examination revealed a height of 1.80 m (a 56 cm increase) with a BMI of 26 kg/m^2, significant muscle mass, no facial dysmorphia, no bilateral adipomastia, a penis size of 12 cm (an 8 cm increase), no abnormalities of the frenulum or induration, atrophic testicles measuring 3 ml, and the presence of pubic and axillary hair.
He was offered weekly HCG injections and daily FSH injections in an attempt to induce spermatogenesis. After 6 months, the spermogram revealed total azoospermia, and the testicular ultrasound still showed bilateral atrophic testicles. The patient decided to discontinue the fertility induction treatment. He reported experiencing depression during this attempt and currently lacks motivation to pursue fertility induction again.

Discussion:-

The epidemiology of PES differs according to the diagnostic method. It is usually found incidentally in 5.5% to 12% of autopsy cases. However, the overall incidence has been estimated to be 12% based on neuroimaging, and around 9–35% based on clinical findings reported in several case serieswith an increasing incidence in the last few decades possibly due to the improvements and availability of neuroimaging techniques[5].The female-to-male ratio of PES is 5:1, and in women, the peak occurrence usually happens between the ages of 30 and 40. It is less common in children and is linked to problems during pregnancy, genetic abnormalities, and hypothalamic-pituitary dysfunction [2].Available data on hypopituitarism in PES are greatly variable, with rates ranging from 19 to 68%. The majority of patients displayed only one deficiency (72%) and central hypogonadism was the most frequent (20%)[9], while other authors found GH deficiency instead as the most common[6-7-8] . A study on PES showed hypogonadotropic hypogonadism as the most common endocrine problem (19%) which presents as oligomenorrhoea in females and decreased sexual function in males[9]. The findings of these studies shows that PES with hypogonadotropic hypogonadism is an uncommon diagnosis in male patients.The diagnosis of PES is based on magnetic resonance imaging (MRI) of the sellar and suprasellar regions. For individuals who are completely contraindicated to MRI, computed tomography (CT) imaging is used to confirm the diagnosis[2].

The cause of PES is uncertain, but possible explanations include:

1. Incomplete formation of the sellar diaphragm
2. Upper sellar factors such as persistent or intermittent intracranial idiopathic hypertension, CSF pulsatility, obesity, or systemic hypertension
3. Pituitary factors, including conditions associated with variations in pituitary volume such as pregnancy, lactation, menopause, hypophysitis, or compensatory pituitary hypertrophy due to primary hormonal deficit [3-4].

Sharavii et al. studied all candidate genes related to the development of PES in humans and divided them into four groups: Group 1- genes, related to the development of PES (the most significant are the PRL gene coding for prolactin, the GH1 gene coding for growth hormone, the POMC gene coding for proopiomelanocortin, the TRH gene coding for thyrotropin releasing hormone, the IGF1 gene coding for insulin like growth factor 1); Group 2- candidate genes related to pathways of PES (TRH, PRL, POMC, NPY, GNRH1, GH1, genes coding for peptide-ligand building receptors); Group 3- candidate genes related to cellular components of PES(PRL, POMC, NPY, IGFBP3, IGF1) and Group 4- candidate genes related to biological processes of PES (TRH, POMC, NPY, INS, GNRH1) which participate in the regulation of biological processes associated with the G protein-coupled receptors signaling pathway[3-4].

Hormone replacement therapy is the course of treatment for these patients. In this instance, testosterone treatment might not increase fertility, but it might aid in the production and preserve virilization and avert hypogonadotropic hypogonadism's long-term consequences, such as osteoporosis and cardiovascular issues, and it is necessary to continue monitoring for any complications related to the substitution[10].

Conclusion:-

We presented a rare clinical case of a male patient with PES and hypogonadotropic hypogonadism, mostly seen late at 30 to 40 years of age and mostly in females. Prompt recognition of prepubertal hypogonadotropic hypogonadism at an early age and early intervention can improve a patient's quality of life. In our case, the management could be more comprehensive if the patient agreed to continue substitution therapy with the aim of inducing fertility.

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