HYPOGONADOTROPHIC HYPOGONADISM WITH SYNKINESIA AND DERANGED PITUITARY PROFILE: AN ENIGMA OF FINDINGS AND DILEMMA IN DIAGNOSIS

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ABSTRACT
A 14-year-old Indian male presented with complaints of growth failure which parents noticed for the last four years & no development of secondary sexual characteristics causing significant parental anxiety. Neurological examination was normal except the child exhibited mirror movements in the upper extremities. MRI (magnetic resonance imaging) of the pituitary & the hypothalamus showed “a pituitary macro-adenoma with supra-sellar extension with chiasmal compression without cavernous sinus involvement”. Our presentation is probably the first case which revealed synkinetic movements in a case of pituitary macroadenoma. At the same time our case calls for a study of the inhibitory association tracts which physiologically prevents mirror movements.

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INTRODUCTION
Hypogonadotropic Hypogonadism (HH) is an uncommon disorder with an estimated incidence of approximately 1-10:100,000 live births; approximately 1/3 and 2/3 of cases are caused by idiopathic hypogonadotropic hypogonadism and Kallmann syndrome (KS) respectively [1]. HH is a genetic disorder and several mutations have been implicated in its pathogenesis [2]. The phenotype is a failure of migration of Gonadotropin-releasing hormone (GnRH) bearing neurons from the olfactory bulb to the hypothalamus [2]. Clinically, there is an overlap with constitutional delay of growth and puberty (CDGP) which can be resolved once the patient is 18 years of age or more [3]. Endocrinological confirmation is by documenting low levels of sex steroids after 18 years age, lack of luteinizing hormone (LH) stimulation with GnRH and by documenting a testosterone response to human chorionic gonadotropin (HCG).

CASE REPORT:
A 14-year-old Indian male presented with complaints of growth failure which parents noticed for the last four years & no development of secondary sexual characteristics causing significant parental anxiety. Our patient received three injections of testosterone outside after a diagnosis of hypogonadotrophic hypogonadism was made which increased his penile length but masculine features were yet to develop. On detailed examination the child had a height of 141.5 cm, falling between the 3rd and 5th percentile. Height SDS was -1.94. Target height SDS was -1.53. Height age was 11 years & bone age was 9 years. Arm span being 144.5 cm. The testicular volume was 2 cm bilaterally & the stretched penile length 7.5 cm without any axillary or pubic hair. (Figure 1)

Figure 1: Gentital examination revealing “a stretched penile length of 7.5 cm without any axillary or pubic hair” most probably due to testosterone supplements patients received during initial treatment

Based on the aforementioned findings a clinical diagnosis of hypogonadotropic hypogonadism was evident. Neurological examination was normal except the child
exhibited mirror movements in the upper extremities. Retrospective enquiry about the movements revealed that the parents noticed such movements in the form that the child had his left hand and fingers moving when he used his right hand to eat but they noticed it only for around 3 years or so. Further evaluation revealed normal intellectual capabilities, no signs of raised intra-cranial tension or anosmia. No significant family history was noted.

The basic hormonal profile of the child depicted hypothyroidism of the central type {Serum TSH (thyroid stimulating hormone) - 2.39 micro IU/ml (normal range -0.7- 4.4), fT4-0.78 ng/dl (normal range 0.8- 2.0 ng/dl), serum prolactin- 8.08 ng/ml, Basal 8 am Serum cortisol – 9.5 microgram/dl. A GnRH (Gonadotropin stimulation test) showed a peak serum LH (luteinizing hormone) value of less than 0.5mIU/ml. An IGF-1 value of 74ng/l prompted for an Insulin Tolerance test. The peak Growth hormone level achieved at 90 minutes was only 0.239 ng/ml. The serum cortisol levels rose from basal 10.5 micro-gram/dL to 10.10 micro-gram/dL at 90 minutes. The profile reveals combined pituitary hormone deficiency with suppression of the entire anterior pituitary axis. We now have a case of combined pituitary hormone deficiency with synkinesia.

With the aforesaid information we went for MRI (magnetic resonance imaging) of the pituitary & the hypothalamus which showed a pituitary macro-adenoma (7mm lateral and 10 mm in cranio-caudal direction) with supra-sellar extension with chiasmal compression without cavernous sinus involvement.(Figure 2)

Figure 2: MRI of the pituitary and the hypothalamus revealing a pituitary macro-adenoma (7mm lateral & 10 mm in cranio-caudal direction) with supra-sellar extension with chiasmal compression without cavernous sinus involvement.
DISCUSSION:

The X-linked form of Kallmann’s syndrome, KAL3 and KAL4 (PROKR2 and PROK2 mutations) usually have associated upper limb synkinetic movements along with dental agenesis & renal agenesis (35-40% cases of X-linked inheritance) \cite{4}. The congenital nature of the aforementioned defect implies that the synkinetic movements are usually present from childhood & does not appear abruptly during adolescence, as in our case where it appeared only in the last three to four years. Keeping aside the synkinetic movements, our case lacks any associated features resembling Kallmann’s. Synkinesia happens in Kallmann due the derangement of the corticospinal tract. Acquired synkinetic movements in a case of pituitary macro-adenoma with combined pituitary hormone deficiency closely mimicking Kallmann’s Syndrome makes the case unique. The cause of synkinesia in a pituitary macro-adenoma still remains unsolved. Other than Kallmann’s, synkinesia has been reported in certain neurological conditions such as Parkinson’s disease (PD), corticobasal syndrome (CBS), essential tremor (ET), focal hand dystonia, Creutzfeldt-Jakob’s disease (CJD), and Huntington’s disease \cite{5}. The common area of involvement in all of the above conditions remains abnormalities in the corpus callosum & Basal Ganglia \cite{4,5}. Existence of the inhibitory neurones of the corpus callosum & basal ganglia, which suppress concomitant discharge from the contra-lateral hemisphere, thus causing bilateral discharge from cerebral cortex on motor motivation of a single hemisphere has been well illustrated \cite{5}. What is not known is the exact pathway of these inhibitory tracts. In the context of our case, we can only speculate that these inhibitory fibres may be compromised by the macro-adenoma resulting in synkinetic movements.

CONCLUSION:

Our presentation is probably the first case which revealed synkinetic movements in a case of pituitary macro-adenoma from India and world literature. At the same time our case calls for a study of the inhibitory association tracts which physiologically prevent mirror movements.

REFERENCES:


