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CASE REPORT

KALLMANN SYNDROME-A RARE CASE REPORT

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ABSTRACT: Kallmann syndrome (KS) is a genetic disorder characterised by hypogonadotrophic hypogonadism and anosmia or hyposmia. The condition has been noted to be present in families. The MRI findings in KS are characteristic and MRI is a useful adjunct to the diagnosis of KS. We are presenting a case of young boy who was short statured and had anosmia with multiple hormonal deficiencies.

KEYWORDS: Kallmann, Anosmia, Hyposmia, Hypogonadotrophic hypogonadism,
Magnetic Resonance Imaging.

INTRODUCTION: Kallmann syndrome is an inherited disorder characterized by hypogonadotrophic hypogonadism and anosmia or hyposmia.[1] Reported incidence is 1 in 10,000 men and 1 in 50,000 women. Kallmann syndrome (KS) is a genetic disorder resulting from impaired physiologic migration of the olfactory and GnRH neurons during embryonic life. Three modes of inheritance have been reported: X-linked recessive, autosomal dominant and autosomal recessive. Approximately 60% of cases with KS are sporadic. Mutations in the KAL1 gene are detected in 14% of familial cases and in 11% of sporadic cases.[2] Apart from KAL1 (Xp 22.3), the genes responsible for the KS phenotype are the KAL2 [fibroblast growth factor receptor 1] (FGFR1) gene (10%) and the KAL4 [Prokinetecin receptor 2] (PROKR2) and KAL3 [Prokinetecin 2] (PROK2) (9%) genes.[3] In addition, the KAL5 [Chromodomain-helicase- DNA binding protein 7] (CHD7) gene and KAL6 [Fibroblast growth factor 8] (FGF8) are also candidate genes for KS Structural olfactory tract abnormalities are well seen on MRI due to high resolution and multiplannar capability.

CASE PRESENTATION: A 24 year old boy presented to department of endocrinology in the month of January 2015 with chief complain of poor development of secondary sexual characteristics and decrease smelling capacity. On USG examination, we found bilateral empty scrotal sac with bilateral small testes (RT-14x4.9mm and 12.8x4.4mm) lying adjacent to superficial inguinal ring. On hormonal examination, we found low level of testosterone (11.52 ng/dl), normal FSH (2.25 mIU/ml), slightly low LH (0.319 mIU/ml), and normal TSH (1.31 mIU/ml), PRL (3.43 ng/ml) and cortisol (6.48 mcg/dl at 8 AM) level. On MRI Examination we found non visualisation of both the olfactory bulb and olfactory nerve. There is associated pituitary hypoplasia with height of the anterior lobe measures 3.7 mm.

DISCUSSION: Kallmann's syndrome is a condition that specifies hypogonadotrophic hypogonadism and anosmia. This clinical condition was first reported by Maestre de San Juan, a Spanish anatomist in 1856. In 1944, Kallmann described a syndrome of primary eunuchoidism secondary to hypogonadotrophic hypogonadism associated with congenital anosmia [1]. Hypogonadism is due to deficiency of gonadotrophin releasing hormone (GnRH) which occurs due to failure of the embryonic migration of neuroendocrine GnRH cells from olfactory epithelium to forebrain.

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Anosmia is related to the absence or hypoplasia of the olfactory bulbs and tracts in most of the cases. Usual presentation is due to abnormal phenotype including micropenis, loss of voice change, absence of definite hair distribution and infertility. Anosmia is usually noted on clinical examination. Different modes of presentation in addition to hypogonadism and anosmia have been reported.

Relevant investigations include serum testosterone levels which are low or absent. Luteinizing hormone (LH) and follicle stimulating hormone (FSH) are low. Other hormonal functions of anterior pituitary may be disturbed. Diminished cortisol response to insulin induced hypoglycemia has been reported.[4]

Testosterone is given as part of replacement therapy to restore virilization and secondary sex characters. In females combined estrogen and progesterone are used. To restore fertility pulsatile treatment with GnRH can be used.[5] other treatment modalities are according to associated clinical problems. Counselling of patient and his family regarding the clinical condition and its management is also important.

CONCLUSION: We report a rare case of Kallmann syndrome presenting with poor development of secondary sexual characteristics and decrease smelling capacity. We did not recognize the condition until radiological and biochemical investigations were performed.

It is necessary to diagnose Kallmann's syndrome, as timely replacement can restore secondary sex characters and fertility. In this way, patient and his family can be saved from a lot of psychosocial problems.

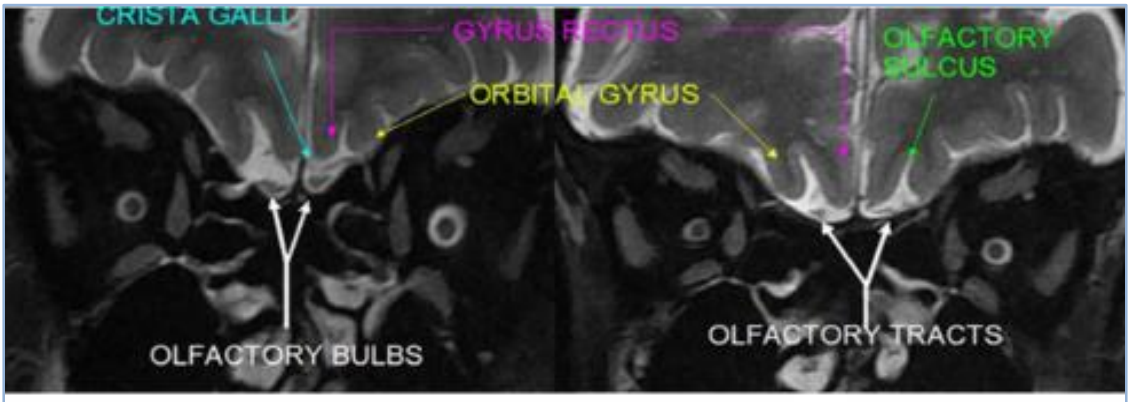

Fig1 : Coronal T2 weighted images of a normal individual showing normal olfactory Bulbs, olfactory sulci, olfactory tracts, gyrus rectus and orbital gyrus

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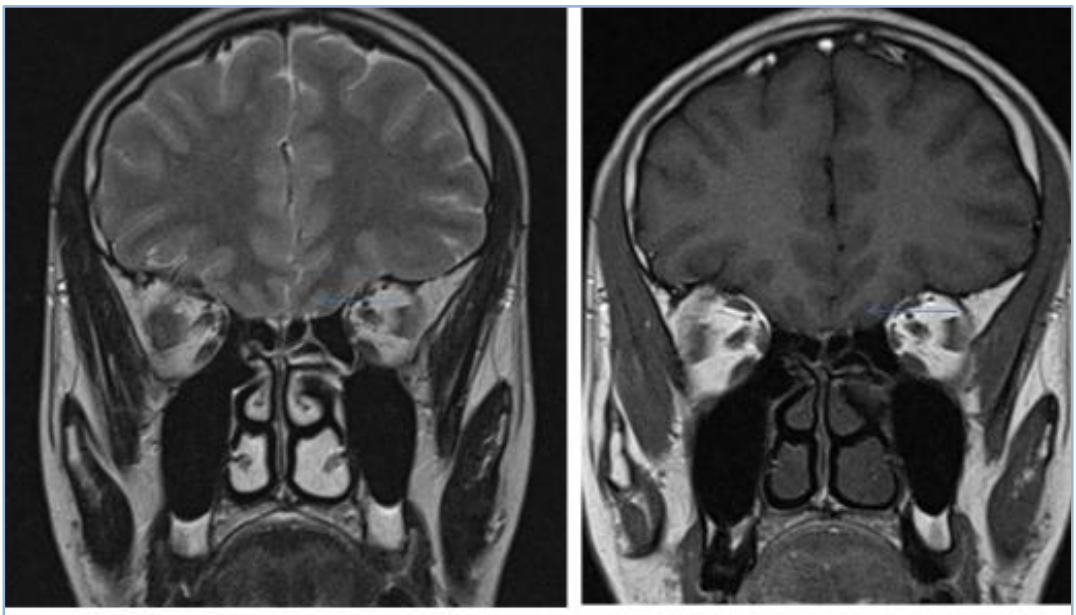
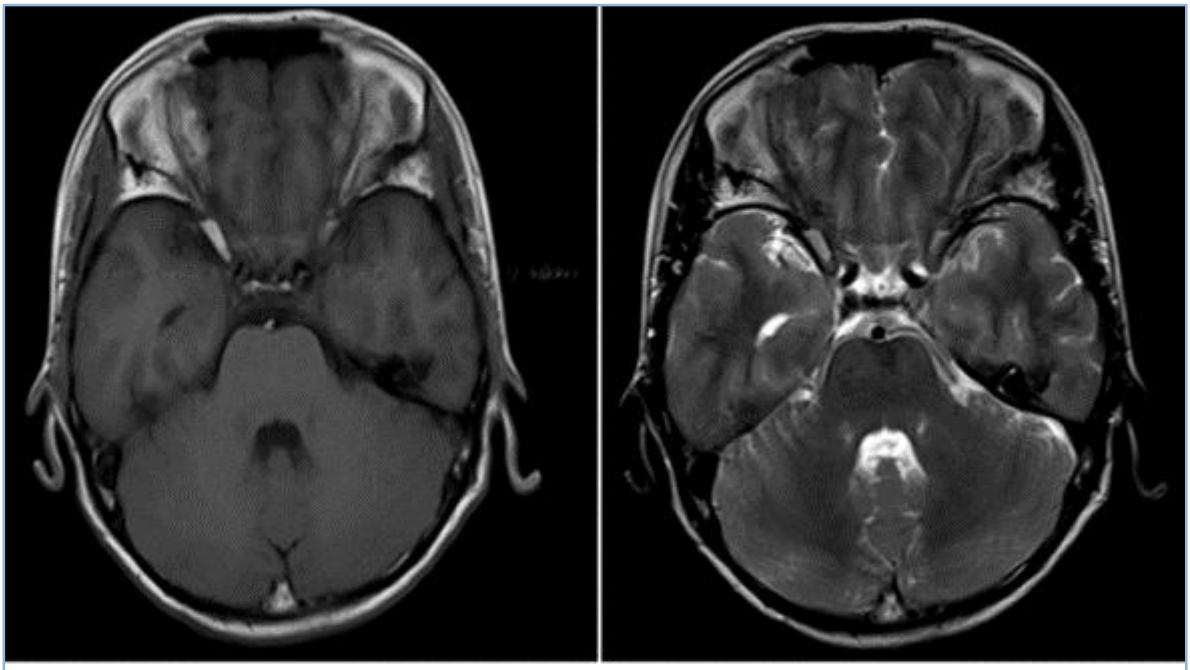


A B

Fig 2: T2(A) and T1 (B) weighted coronal image of the patient shows absence of olfactory sulcus (arrows). There is absence of olfactory bulbs.



A B

Fig 3: T2(A) and T1 (B) weighted axial image of the patient shows absence of bilateral olfactory sulci.

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