Case Report

MRI findings in Kallmann syndrome

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Kallmann syndrome (KS) is a neuronal migration disorder characterised by hypogonadotrophic hypogonadism and anosmia or hyposmia. Five patients with clinical findings suggestive of KS were evaluated with MRI. All patients had abnormalities of olfactory system. Olfactory bulbs were absent in all patients. Olfactory sulci were absent in 3 patients and hypoplastic in 2 patients. Anterior pituitary was hypoplastic in two patients. The MRI findings in KS are characteristic and MRI is a useful adjunct to the diagnosis of KS.

Key Words: Kallmann syndrome, Hypogonadotrophic hypogonadism, Anosmia, Magnetic Resonance Imaging, Olfactory system.

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. KS is due to abnormal migration of gonadotropin-releasing hormone (GnRH) as well as olfactory neurons from olfactory placode to the forebrain and hypothalamus during fetal life. This is secondary to failure of genetic expression of cell markers that guide migrating neurons.[2,3] Structural olfactory tract abnormalities are well seen on MRI due to high resolution and multiplannar capability. We present MRI findings in five cases of KS.

Case History

Five male patients (Age range 21-34 years) with clinical findings suggestive of KS were evaluated with MR imaging. All patients had anosmia and hypogonadotrophic hypogonadism. (Serum LH < 1.5 IU/L, Serum FSH < 1.5 IU/L, Testosterone <20 ng/dl). GnRH stimulation test was not performed, as the clinical picture was compatible with KS. All studies were performed on 1.5 T GE (Signa) scanner. MRI sequences included coronal T1 (TR/TE 600/15) and T2 W (TR/TE 4500/90) images from the anterior margin of the frontal sinus to the hypothalamus. Images were obtained at 3 mm thickness with 0.3 mm interslice gap. In addition axial T1, T2W and sagittal T1W images were obtained. The olfactory sulci and bulbs were assessed as normal, hypoplastic or absent. (Sulci were assessed as hypoplastic in comparison to rest of cerebral sulci). Pituitary gland was also evaluated and anterior pituitary was assessed as normal or hypoplastic (Height < 4 mm).[4]

Abnormalities of olfactory sulci and bulbs were noted in all 5 patients (Table 1). All patients had absent olfactory bulbs (Figures 1, 2 and 3). Olfactory sulci were absent in 3 patients (Figure 2) and hypoplastic in 2 patients (Figure 4). Anterior pituitary was hypoplastic in 2 patients (Figure 4). Posterior pituitary appeared normal in all patients. There was no correlation of imaging findings with the

Table 1: MRI findings in Kallmann syndrome

Patient	Age	Sex	Olfactory sulci	Olfactory bulbs/Tracts	Anterior Pituitary
1	22	M	Absent	Absent	Normal
2	34	M	Absent	Absent	Normal
3	35	M	Hypoplastic	Absent	Hypoplastic
4	26	M	Hypoplastic	Absent	Hypoplastic
5	21	M	Absent	Absent	Normal

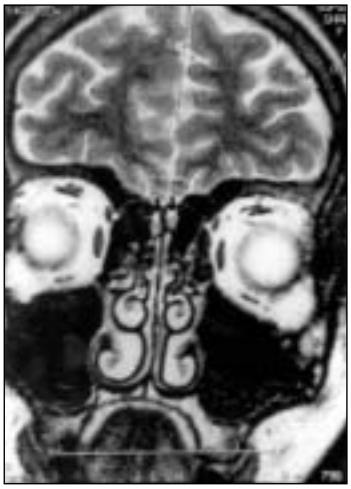

Figure 1: Coronal T2 Weighted image shows normal olfactory bulbs (arrows)

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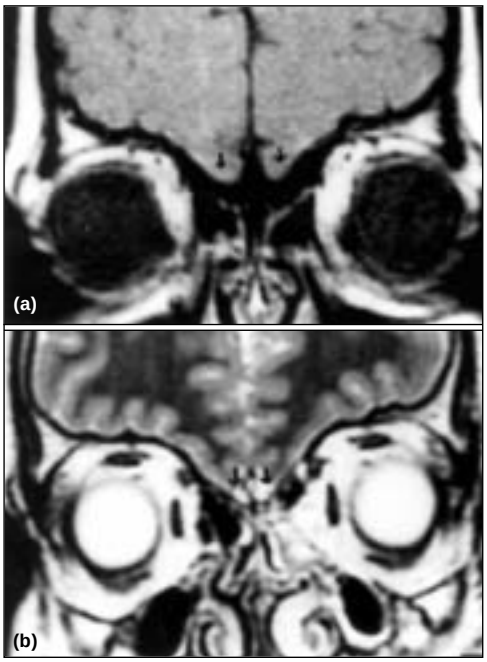

Figure 2: Coronal T1 (a) and T2 (b) weighted images of 21 year old patient with KS demonstrate absent olfactory sulci (arrows in a) and olfactory bulbs (arrows in b)

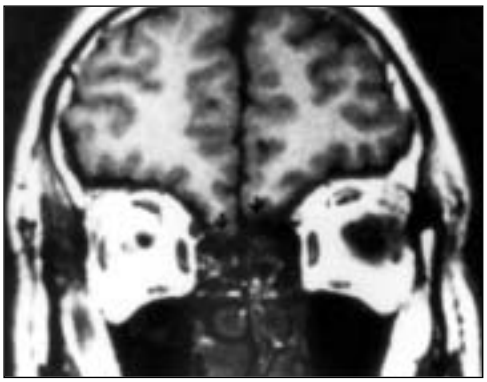

Figure 3: Coronal T1 Weighted image of 34 year old male patient reveal absent olfactory bulbs (arrows)

degree of anosmia and hypogonadism.

Discussion

KS is an association of olfactory and genital abnormalities, which was first noted by Mastre de san Juan in 1856. In 1944, Kallmann described a syndrome of primary eunuchoidism secondary to hypogonadotrophic hypogonadism associated with congenital anosmia.[1] Kallmann syndrome is an anomaly of neuronal migration. Cells that differentiate into Gonadotrophin releasing hormone (GnRH) secreting neurons originate from within embryonic olfactory epithelium and migrate along fascicles of vomeronasal and terminalis nerves into forebrain.[3] This migration of GnRH neurons is arrested in KS resulting in GnRH deficiency followed by different degrees of luteinizing hormone (LH) and follicle stimulating

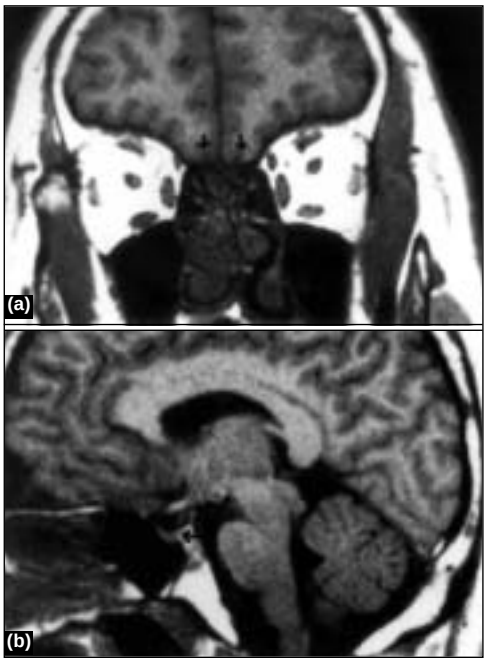

Figure 4: Coronal T1 Weighted image (a) shows hypoplastic olfactory sulci (arrows in a). The olfactory sulci lie between Gyrus rectus and Medial orbital gyrus. Sagittal T1 weighted image shows (b) hypoplastic anterior pituitary gland (arrow)

hormone (FSH) deficiencies.[3] Abnormal development of olfactory placode also results in improper development of olfactory bulbs and sulci. Other associated anomalies including various cardiovascular abnormalities, renal agenesis, cryptorchidism, short fourth metacarpal and facial anomalies have been reported in-patients with KS.[5] In none of our patients, other anomalies were noted.

Morphological abnormalities of olfactory apparatus in KS are best evaluated with MRI. Suzuki et al was the first to describe the visualization of olfactory bulbs and tracts on MR scans.[6] Olfactory bulbs are optimally visualized in coronal planes. Olfactory bulbs are seen as well-defined structures along cribriform plate. Olfactory sulci are seen between Gyrus rectus and medial orbital gyrus. High resolutions coronal fast spin echo T2W and T1W images are the preferred sequences for morphologic evaluation of the olfactory system.[7-9] Reported abnormalities include hypoplastic/aplastic olfactory sulci and olfactory bulb.[7-12] In our study, all patients had abnormalities involving olfactory sulci and olfactory bulb. In addition, two patients had hypoplastic anterior pituitary gland. Hypoplasia of anterior pituitary may be secondary to limited stimulation due to absence of hypothalamic GnRH neurons.

Clinical diagnosis of KS in adults is fairly straightforward, depending on the co-existence of anosmia with subnormal levels of gonadal steroids and gonadotrophins. However the diagnosis may be difficult to establish in-patients of pre-pubertal age who may require genetic testing and MRI. In such patients, MRI enables a presumptive diagnosis of KS to be made by demonstrating characteristic abnormalities in olfactory sulci and tracts.

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