

Picture Stories

Kallmann syndrome with characteristic magnetic resonance imaging findings

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Introduction

Kallmann syndrome (KS) is a neuronal migration disorder characterised by hypogonadotropic hypogonadism associated with anosmia or hyposmia. It affects males more than females with a male to female ratio of around 6:1¹. We report a rare case of Kallmann syndrome with delayed puberty, anosmia and characteristic magnetic resonance imaging (MRI) findings.

Case report

A 14 year old boy of normal intelligence presented with delayed puberty and anosmia since childhood without a similar history in the family. Physical examination revealed a height of 154.5 cm (more than 10th centile), arm span of 159 cm and a stretched penile length (SPL) of 3.5 cm. Bilateral testicular volume was pre-pubertal around 2 cc. (Puberty-4 cc, adult-12.5 to 19 cc) with sparse pubic hair (Tanner's staging G1P2)². Hormonal work up revealed inappropriately low luteinising hormone (LH) 0.07 mIU/ml (Male: 1.5-9.3) and follicle-stimulating hormone (FSH) 1.05 mIU/ml (Male: 1.6-8.0). 8 A.M. testosterone was 70 ng/dl (Male: 300-1000ng/dl)^{3,4}. LH-releasing hormone stimulation test was planned but could not be done. Karyotyping confirmed 46 XY. Bone age corresponded to chronological age. All other investigations including thyroid profile, serum cortisol, prolactin level, and hearing test were within normal range. Thus, this patient was diagnosed as

hypogonadotropic hypogonadism. With background history of anosmia since childhood, our diagnosis was Kallmann syndrome. For further evaluation we did MRI of brain, which revealed absent olfactory bulb and tract in anterior sections and also absence of olfactory sulcus (OS). The medial orbital gyrus (MOG) and gyrus rectus (GR) were fused. (Figures 1 and 2).

Discussion

Male patients usually present in the second decade with failure to start or fully complete puberty and have the additional symptoms of hypogonadism and almost invariably infertility. Females usually present with primary amenorrhoea. Pre-pubertal boys sometimes may present with micropallus and cryptorchidism⁵. Although anosmia is present since birth it is usually not apparent. They may also exhibit bimanual synkinesis i.e. simultaneous movement of both hands which is mainly seen in inherited KS⁶. Symptoms of associated congenital heart disease or neurologic manifestations may be present. Rarely patients may have one kidney and features of osteoporosis⁷.

Regarding inheritance, Kallmann syndrome may be sporadic or can be inherited as three modes, X-linked, autosomal dominant and autosomal recessive. X-linked form is the most common and the responsible gene is KAL1 that encodes the protein anosmin which is directly responsible for the migration of gonadotrophin releasing hormone (GnRH) neurons and the olfactory nerves from the olfactory system to the hypothalamus. Patients with KS, therefore, suffer both reproductive and olfactory dysfunction. The next common inheritance is the autosomal dominant form due to a mutation of the KAL2 gene on chromosome 8. The third inherited form is autosomal recessive due to the mutation of the KAL3 gene. The exact location of the KAL3 gene has not yet been discovered⁸⁻¹¹.

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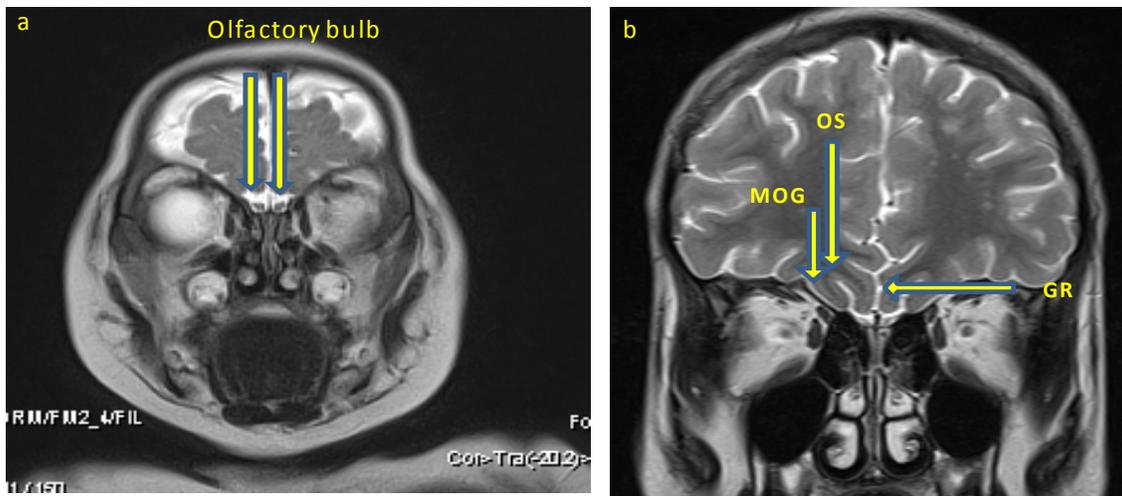


Figure 1: Cranial magnetic resonance imaging of the olfactory bulb region in a control man

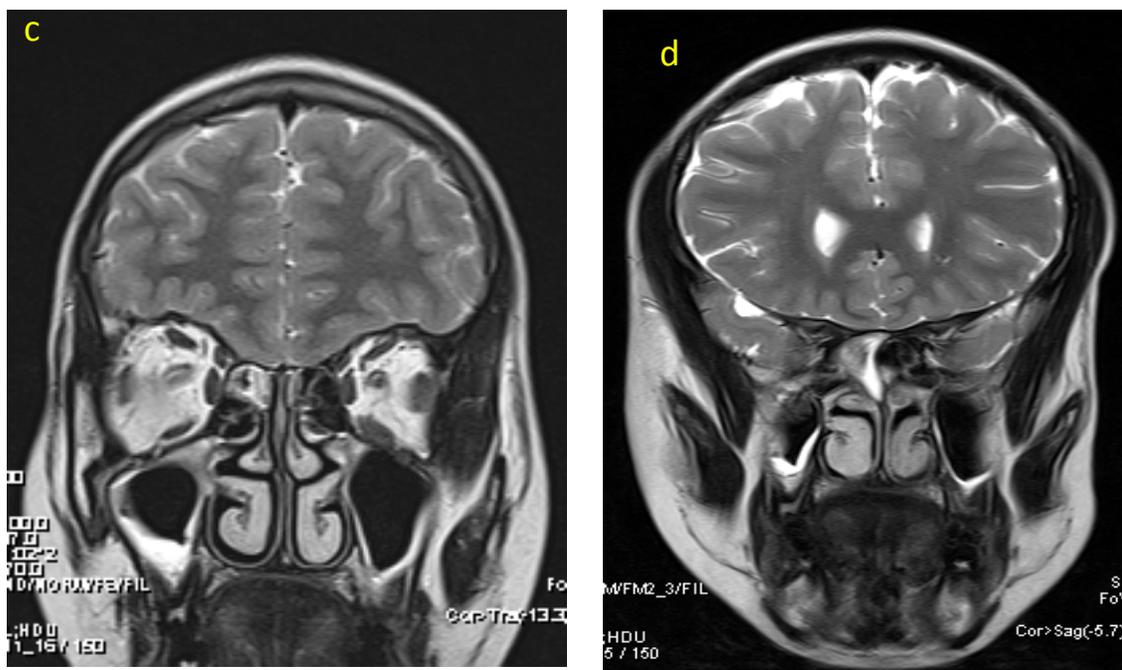


Figure 2: Cranial magnetic resonance imaging of the olfactory bulb region in Kallmann syndrome

Molecular pathogenesis says that there is impaired development of olfactory axon and the migration of GnRH neurons that fail to migrate from the medial olfactory placode into the forebrain. There is also failure of neuronal migration from the lateral olfactory placode to the forebrain resulting in aplasia or hypoplasia of the olfactory bulbs and tracts, which can be evaluated in MRI (Figure 2)¹².

MRI of brain is an important tool. To look at the olfactory bulbs and tracts, study of more anterior and thin coronal sections on T2W, MR images are important. As KS is a neuronal migration disorder, associated abnormalities like fusion of gyrus rectus and medial orbital gyrus, shallow or absent orbital

sulcus may be evident. MRI can also show a possible associated brain abnormalities¹³.

Medical treatment can reverse the problem of hypogonadism and the management aims for normal reproductive health. Replacement of the missing hormones is the main focus. For the male, testosterone can be given as Injection Slow-release skin patch or gels and for the female oestrogen and progesterone pills which help to develop secondary sexual characteristics. When fertility is required Pulsed gonadotrophin releasing hormone is administered, which has a complex schedule with variable success^{14,15}.

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