A 14-year-old boy presented to the out-patient clinic with poorly developed secondary sexual characteristics. He had undergone bilateral orchidopexy for undescended testes 5 years earlier. On physical examination, his height was found to be at the 20th centile of normal. His body mass index was 26.3 kg/m$^2$. He had poorly developed secondary sexual characteristics and infantile testes (1 mL) but did not have eunuchoid proportions. His olfactory sensation was impaired. His serum follicle-stimulating hormone (FSH) and luteinising hormone levels were 0.16 mIU/mL and <0.10 mIU/mL, respectively and his testosterone levels were also low. Figure 1 shows the brain magnetic resonance image (MRI brain) of a normal individual. What structures do the arrows indicate? The MRI brain of the above patient is shown in Figure 2. What abnormality is seen? What is the probable diagnosis?

**Discussion**

This patient had undescended testes and poorly developed secondary sexual characteristics associated with hyposmia and low gonadotrophin levels. A diagnosis of Kallmann’s syndrome was considered. Figure 1 shows a normal MRI where the curved arrow indicates the olfactory sulcus and the straight arrow indicates the olfactory bulb. These structures are clearly absent in Figure 2, a feature of Kallmann’s syndrome.

Kallmann’s syndrome is a rare form of idiopathic hypogonadotrophic hypogonadism, which presents with features of hypogonadism and hyposmia. A diagnosis of Kallmann’s syndrome cannot be made until other structural pituitary and hypothalamic causes of hypogonadotrophic hypogonadism have been excluded. The prevalence of Kallmann’s syndrome has been reported as 1 in 86,000 men among military recruits. Many cases are sporadic, representing new mutations. Familial cases may be autosomal dominant, autosomal recessive, or X-linked. The X-linked form may be associated with mutations in the KAL gene (Xp22.3), which encodes anosmin-1, a neural cell adhesion molecule necessary for the migration of olfactory neurone axons and gonadotrophin-releasing hormone (GnRH) synthesising neurones toward their final location. Loss-of-function mutations of the gene encoding FGFR1 (fibroblast growth factor receptor-1, 8p12), a tyrosine kinase receptor involved in cell differentiation and embryogenesis have been implicated in patients with autosomal dominant Kallmann’s syndrome. FGFR1 is found in the olfactory placode of human embryos and is necessary for the migration of GnRH-expressing neurones towards the hypothalamus.

Patients usually report partial or no pubertal maturation. Females usually present with a history of primary amenorrhoea. Males may present with cryptorchidism and poor sexual development.

Magnetic resonance imaging usually shows complete agenesis of olfactory bulbs and sulci or shallow or medially oriented olfactory sulci, if present. One study comparing the phenotypic characteristics of patients with Kallmann’s syndrome with their radiological characteristics showed that up

---

**FIG 1.** T2-weighted magnetic resonance imaging of the brain of a normal individual

**FIG 2.** T2-weighted magnetic resonance imaging of the patient’s brain
An interesting case of hypogonadism

Hong Kong Med J Vol 14 No 3 June 2008 www.hkmj.org

References


to 25% of patients may have olfactory bulbs and sulci, though the sulci are usually medially oriented.4 Treatment includes administration of sex hormones, aiming to achieve normal sexual development. Sex hormones also retard development of osteoporosis, which is common in these patients. Pulsatile administration of gonadorelin (GnRH) restores pituitary-gonadal axis function and fertility in most patients. Gonadotrophins (eg FSH, human chorionic gonadotrophin) have also been used successfully for treatment. The patient discussed above was treated with testosterone injections weekly. His secondary sexual characteristics developed adequately although his testicular size remained infantile.

Deepti Gurdasani, MB, BS
Department of Medicine
Narayanan RS Surendrababu, DMRD, DNB
Department of Radiology
Thomas V Paul, MD, DNB
E-mail: thomasvpaul@yahoo.com
Department of Endocrinology
Christian Medical College and Hospital
Vellore, Pin: 632 004
Tamil Nadu, India

Deepti Gurdasani, MB, BS
Department of Medicine
Narayanan RS Surendrababu, DMRD, DNB
Department of Radiology
Thomas V Paul, MD, DNB
E-mail: thomasvpaul@yahoo.com
Department of Endocrinology
Christian Medical College and Hospital
Vellore, Pin: 632 004
Tamil Nadu, India

Deepti Gurdasani, MB, BS
Department of Medicine
Narayanan RS Surendrababu, DMRD, DNB
Department of Radiology
Thomas V Paul, MD, DNB
E-mail: thomasvpaul@yahoo.com
Department of Endocrinology
Christian Medical College and Hospital
Vellore, Pin: 632 004
Tamil Nadu, India