CASE REPORT

One-year-old male with accelerated growth and development

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A 1-year-old male child with isosexual central (gonadotropin-dependent) precocious puberty caused by hypothalamic hamartoma is reported. Details of the diagnosis based solely on neuromaging characteristics, and satisfactory results of medical treatment with gonadotropin releasing hormone agonist analogues, are highlighted.

A 1-year-old male child with a history of accelerated growth and development since the age of 5 months was brought to hospital by his parents. On examination his height was 86 cm (+4 SD); the pubic hair were stage II (Marshall and Tanner); the phallus measured 3.5–10 cm (average prepubertal length 6.2 cm); the testicular volume was 8 ml for each testis (normal prepubertal testicular volume 1–3 ml); and the scrotal skin was thinned and wrinkled. The bone age was 3 years 6 months. The results of hormone evaluation are presented in table 1.

A cranial magnetic resonance imaging (MRI) scan was undertaken. The contrast enhanced sagittal T1 image (fig 1) shows a 25 mm diameter well defined non-enhancing iso-intense to grey sessile mass interposed between the pons and infundibulum and projecting into the suprasellar cistern (arrow). The axial fluid attenuated inversion recovery (FLAIR) image (fig 2) shows that the mass is mildly hyperintense on T2 weighted imaging (arrow). The imaging characteristics are consistent with hypothalamic hamartoma. The infant's serum gonadotropins and testosterone concentrations are pubertal. On luteinising hormone releasing hormone (LHRH) stimulation, the maximum luteinising hormone (LH) peak over baseline was 26.7 IU/l (>25.5 IU/l pubertal response). The patient was diagnosed with isosexual central (gonadotropin-dependent) precocious puberty caused by hypothalamic hamartoma.

The patient was managed with a long acting gonadotropin releasing hormone agonist analogue (leuprolide acetate 3.75 mg), administered by subcutaneous injection once a month. There was a deceleration of growth velocity and skeletal maturation. The testicular volume regressed to prepubertal concentrations over the next 5 months. There was no increase in size of the hypothalamic mass on repeat MRI 6 months later.

Table 1 Results of hormone evaluation

Hormone	Patient	Normal
Serum testosterone	47.35 nmol/l	Men 10–35 nmol/l, prepubertal 0.17–0.61 nmol/l
Serum DHEAS	1800 µg/l	500–2500 µg/l
LHRH stimulation	LH increase from 1.9 IU/l to 28.6 IU/l	0.9–15 IU/l, prepubertal 1.0–5.9 IU/l
	FSH increase from 4.2 IU/l to 32.8 IU/l	Men 1.3–13 IU/l

DHEAS, dehydroepiandrosterone sulfate; FSH, follicle stimulating hormone; LH, luteinising hormone; LHRH, luteinising hormone releasing hormone.

Figure 1 Contrast enhanced sagittal T1WI image.

Figure 2 Axial FLAIR image.

The child is now receiving regular treatment and follow-up examinations at the endocrinology outpatient department.

DISCUSSION

Several forms of intracranial lesions have been implicated in the aetiology of central precocious puberty, the most common being a hypothalamic hamartoma—a heterotopic mass located typically in the region of tuber cinereum. This congenital malformation consists of gonadotropin releasing hormone (GnRH) secreting neurons believed to function together as an ectopic pulse generator, escaping the normal central nervous system (CNS) inhibitory constraints on pubertal onset. Hypothalamic hamartoma may directly secrete GnRH, since GnRH has been located histochemically within hamartomatous neurons. Hypothalamic hamartoma may be associated with an increased incidence of seizures, particularly laughing seizures, and psychomotor delay. Medical treatment with long acting

Abbreviations: CNS, central nervous system; FLAIR, fluid attenuated inversion recovery; GDPP, gonadotropin dependent precocious puberty; GnRH, gonadotropin releasing hormone; LH, luteinising hormone; LHRH, luteinising hormone releasing hormone; MRI, magnetic resonance imaging

Learning point

Diagnosis of hypothalamic hamartoma is suggested by the presence of early onset (<2 years) isosexual central precocious puberty, especially if associated with laughing seizures without focal neurological signs, and in the presence of a hypothalamic mass, with typical imaging characteristics determined by MRI studies. The hypothalamic mass does not enlarge over time, and has the characteristic hormonal findings of puberty. It behaves benignly and responds satisfactorily to medical treatment with GnRH analogues.

GnRH analogues effectively suppresses gonadotropin secretion and controls premature pubertal development.¹

Before the 1980s the diagnosis of a small hypothalamic hamartoma was difficult using neuroimaging studies. A definite diagnosis was based on pathological study of the mass. MRI scanning is a more sensitive procedure in distinguishing hypothalamic hamartoma from CNS mass lesions such as hypothalamic glioma, ganglioneuroma, ependymoma, or astrocytoma, which feature in its differential diagnosis.² In a series of 70 patients with gonadotropin dependent precocious puberty, eight patients were diagnosed with hypothalamic hamartoma based on MRI.³ MRI is superior to computed tomographic scanning in the identification of a hypothalamic hamartoma. T1 weighted images demonstrate a lesion as isointense compared to the grey matter. On T2 weighted images hypothalamic hamartoma is hyperintense in relation to the grey matter.³ On MRI scan the morphological nature of hypothalamic hamartoma can be clearly defined. Biopsy with its attendant morbidity and mortality is thus avoided for diagnostic purposes.⁴⁻⁵ Surgical resection of the hypothalamic hamartoma is indicated only in cases of progressive

neurological deficit, hydrocephalus, and progressive enlargement of the mass and intractable seizures.³

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