Short reports

Diabetes insipidus and occult intracranial tumours

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SUMMARY We describe four patients with intracranial tumours who presented with diabetes insipidus and subsequently developed an evolving anterior pituitary endocrinopathy. The delay in imaging the tumours varied between 2.1 and 11.2 years (mean 5.4 years).

Most pituitary endocrine deficiencies of childhood are idiopathic,¹ but central nervous system lesions² as well as idiopathic disease may produce a progressive loss of pituitary function with time (evolving endocrinopathy). The association of diabetes insipidus with evolving anterior pituitary endocrinopathy is sinister and points to the presence of an hypothalamopituitary tumour;¹ such tumours usually manifest their presence within four years of the onset of diabetes insipidus.³

We present four cases of diabetes insipidus secondary to occult intracranial tumours and discuss features that may help diagnosis.

Case reports

Case 1. This girl was referred when aged 11.8 years because of secondary enuresis and polydipsia from the age of 3 years and the onset of growth failure between 6 and 7 years. At 12.2 years (Table) an inadequate growth hormone response to insulin

induced hypoglycaemia (peak growth hormone <1 mU/l) was produced in addition to an abnormal plasma thyroid stimulating hormone (TSH) response to intravenous thyrotrophin releasing hormone (TRH) (basal TSH 5.0 mU/l, rising to 16 mU/l at 20 minutes and 22 mU/l at 60 minutes after TRH 200 µg). Secretion of gonadotrophin, prolactin, and cortisol was normal. Fundoscopy, visual fields, skull x ray, and computed tomography of the hypothalamopituitary region showed no abnormality. She was treated with human growth hormone and 1-deamino-8-D-arginine vasopressin (DDAVP). On this regimen her growth accelerated from 2.3 to 8.7 cm/year. At 14.2 years she remained prepubertal. Morning plasma cortisol concentration was low (140 nmol/l at 0800h), indicating adrenocorticotrophic hormone (ACTH) deficiency, and serum thyroxine concentrations (55 nmol/l) had fallen below normal. Fundoscopy, visual fields, and skull x ray remained unchanged, but a further computed tomogram revealed a small hypothalamic tumour, which was treated by radiotherapy without biopsy examination. Puberty was induced by administration of oestrogen and a computed tomogram, at 17 years, showed no evidence of a tumour.

Case 2. This boy presented at 6.6 years of age with an 18 month history of polyuria and polydipsia. Height was on the 50th centile with a normal growth velocity. Plasma cortisol (900 nmol/l) and serum

Table Clinical and endocrine data for four patients with diabetes insipidus due to intracranial tumours

Case No	Sex	Age at onset of diabetes insipidus (years)	Age at onset of growth failure (years)	Age at detection of anterior pituitary endocrinopathy (years)				Age at diagnosis of intracranial tumour (years)	Delay from symptoms to diagnosis (years)
				Growth hormone	TSH	ACTH	Gonadotrophins		
1	F	3.0	6 to 7	12.2	12.2	14.2	14.2	14.2	11.2
2	M	5.1	Normal growth	Normal	6.6	8.0	?	8.0	2.9
3	F	6.7	6.7	7.7	12.2	12.2	12.2	12.2	5.5
4	F	6.0	7.0	7.3	8.1	8.1	?	8.1	2.1

ACTH=Adrenocorticotrophic hormone; TSH=Thyroid stimulating hormone.

growth hormone (>40 mU/l) responses to insulin induced hypoglycaemia were normal. Plasma TSH showed an abnormal response, however, to intravenous TRH (basal TSH <1 mU/l, rising to 3.7 mU/l at 20 minutes and 5.7 mU/l at 60 minutes), although serum thyroxine concentration (73 nmol/l) was normal. Computed tomography of the hypothalamic-pituitary region showed no abnormality. Treatment was begun with DDAVP. At 8 years a low morning plasma cortisol concentration (150 nmol/l at 0800h) indicated probable ACTH deficiency, but secretion of growth hormone was normal. Skull x ray showed enlargement of the pituitary fossa, and a small suprasellar mass was shown on computed tomography. Transsphenoidal exploration revealed a craniopharyngioma, which was partially resected, and radiotherapy was administered postoperatively.

Case 3. This girl presented at 6.7 years with diabetes insipidus and growth failure. Growth hormone deficiency (peak <1 mU/l) was shown in response to hypoglycaemia; other tests of anterior pituitary function, including serum prolactin, were normal, as were computed tomograms at 7, 7.5, and 8 years of age. At 9 years an air encephalogram and further computed tomogram (Figure) were normal. When aged 10 years she began treatment with human growth hormone, and although she remained prepubertal, her growth rate accelerated from 2.9 to 6.4 cm/year. At the age of 12 she was investigated because of headaches and growth arrest while on treatment with human growth hormone. Endocrine assessment revealed ACTH deficiency (plasma cortisol 130 nmol/l at 0800h), abnormal response to intravenous TRH (basal TSH 1.8 mU/l, rising to 24 mU/l at 20 minutes and 69 mU/l at 60 minutes), and

hyperprolactinaemia (serum prolactin 1540 mU/l). Examination of her visual fields showed bitemporal hemianopia with a red target. Skull x ray was unchanged but a further computed tomogram (Figure) showed a tumour of the third ventricle. She was treated with radiotherapy without biopsy examination.

Case 4. A girl of 7.2 years was referred with a 1.2 year history of polydipsia, polyuria, and growth failure. Impaired secretion of growth hormone (peak 12 mU/l) was obtained in response to hypoglycaemia, but no other anterior pituitary dysfunction was shown. Fundoscopy, visual fields, and skull x ray film yielded normal results. She was treated with DDAVP. At 8.1 years her growth had decelerated to less than 2 cm/year. Repeat pituitary function tests showed that her endocrine state had altered. Her peak growth hormone response to hypoglycaemia was only 3.6 mU/l and in addition there was an inadequate plasma cortisol response (peak 210 nmol/l). Serum thyroxine concentration (48 nmol/l) was subnormal. A lateral skull x ray film showed no abnormality, but an air encephalogram showed a suprasellar mass, which was inoperable at surgery, and no biopsy examination was performed. Cranial irradiation was given postoperatively. At age 12.6 years a tumour recurrence was treated by insertion of a ventricular-atrial shunt and further cranial irradiation. Unfortunately, she developed spinal metastases and died at 13 years.

Discussion

All four patients had diabetes insipidus and subsequently showed an anterior pituitary endocrinopathy that evolved with time. The endocrinopathy may have been underestimated by the difficulty in diagnosing gonadotrophin deficiency in prepuberty. We emphasise the necessity to reassess anterior pituitary function with time. Growth response to treatment with human growth hormone may be unimpaired (cases 1 and 3) in the presence of an untreated intracranial tumour, although this response may be temporary (case 3). In one patient impairment of growth while on treatment with human growth hormone and the development of a visual field defect provided clues to the diagnosis, while in the other three children the diagnosis was made on follow up neuroradiology. One patient (case 2) was unusual in having neither growth failure nor growth hormone deficiency.

Initial neuroradiology, which included computed tomography in three patients, yielded normal results. The subsequent imaging of an intracranial tumour was made on the basis of change in the

Figure Enhanced computed tomogram (EMI) images in horizontal section from case 3 at the level of the third ventricle. The image on the left was taken at age 9 years, that on the right at 12 years when an enhancing lesion in the region of the third ventricle (arrow) was imaged.

lateral skull x ray film in one patient or by changes in the computed tomogram or air encephalogram in the other three patients. Case 3 required five sequential computed tomograms and an air encephalogram during a period of 5.5 years before the tumour was imaged. In two of our patients (cases 1 and 3) the interval between the onset of symptoms and diagnosis was greater than four years,³ and in one this delay was 11.2 years. This delay occurred in spite of the recent technological advances in neuro-radiological imaging.

These cases illustrate the importance of both endocrine and neuroradiological follow up in children with apparently isolated diabetes insipidus, particularly if the risk of permanent visual loss due to a tumour is to be avoided. While diabetes insipidus may be familial⁴ or associated with other congenital abnormalities of the brain,⁵ the more usual aetiologies are those of intracranial tumour or histiocytosis. The onset of diabetes insipidus in mid-childhood—especially if combined with growth failure—should never be considered idiopathic. Such cases require careful follow up using high resolution computed tomography⁶ and possibly

nuclear magnetic resonance imaging, if necessary into adult life.

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Height in epilepsy

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SUMMARY Longitudinal data on the height of pre-pubertal children with epilepsy are presented. Although both seizures and antiepileptic drugs may affect serum hormone concentrations, linear growth remains normal.

Serum hormone concentrations can be affected by both seizures¹ and antiepileptic drugs.² Suboptimal adult height after somewhat early puberty has been reported in children who attended a residential school because of epilepsy.³ We report on the stature of children with chronic seizure disorders who live at home and attend local schools.

Patients and methods

The medical records of all children with epilepsy who attended the paediatric neurology clinic at our hospital between May and July 1985 were examined. The present data relate to 51 children (29 girls) who

had been assessed when aged 2 to 11 years. Clinical details are given in the Table. Measurements for standing height, using a Harpenden Stadiometer, were available at six monthly intervals. Data from boys and girls were analysed separately.

As calculation of mean trends in mixed longitudinal data, based on mean values at each age, gives inefficient estimates⁴ the age at which the largest numbers of children were measured was selected (8.0 years for girls and 9.5 years for boys) and the mean heights at this age calculated. Individual increments in height were calculated for each six months and the mean increment successively added to or subtracted from the mean height referred to previously.⁵ This method obviates bias effects from single height measurements from unusually tall or short children. More boys and girls were older rather than younger than the reference age. Data were available at 11 years for 14 boys and 10 girls. The parental heights were ascertained in eight cases in whom seizures had been life long and measurements were available at 11 years.