Cushing's disease and craniopharyngioma

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Summary A 14 year old girl presented with growth failure and Cushing's disease. Histological examination confirmed a craniopharyngioma but failed to show that the tumour secreted adrenocorticotrophic hormone. We suggest that her Cushing's disease was caused by hypothalamic dysfunction associated with increased corticotrophin-releasing hormone secretion, secondary to the craniopharyngioma.

Craniopharyngiomas usually present with symptoms and signs of increased intracranial pressure or localising neurological signs, or both; some, however, present with failure of growth and puberty due to progressive loss of hypothalamic-pituitary function. We describe a girl who had a craniopharyngioma and presented with the sequelae of pituitary hypersecretion of adrenocorticotrophic hormone (ACTH).

Case report

A girl presented at the age of 14-2 years with short stature. Her height was 3-6 standard deviations below the mean for her age, and her skeletal maturation was retarded by two 'years'. The normal consonance of growth and puberty had been lost and her growth rate was only 3 cm a year, although she had attained stage 2 breast development; this suggested an endocrine abnormality. Investigation showed a normal female karyotype, normal thyroid function (serum thyroxine 144 nmol/l), and normal tomograms of the pituitary fossa. The 0900 h plasma cortisol concentration was 540 nmol/l. In response to insulin induced hypoglycaemia, plasma cortisol rose to a peak of 750 nmol/l and the serum growth hormone concentration increased from 3-4 to 21 mU/l (normal peak >20 mU/l).

At 15-3 years her diurnal plasma cortisol concentrations suggested loss of normal diurnal rhythm, with morning and midnight concentrations of 335 nmol/l and 225 nmol/l, respectively (range <120 nmol/l at midnight). These samples were, however, drawn during the first 24 hours in hospital and the results were attributed to stress.

At 16-3 years she had Cushingoid facies, hirsuties, increasing central obesity, spider naevi, and persistent growth failure. She was hypertensive with diastolic blood pressure consistently 90 mm Hg. She had no defects of her visual fields, even on testing with a red target. Plasma potassium concentration was at the lower limit of normal (3-5 mmol/l). The 0800 h plasma cortisol concentration was 731/nmol/l with a plasma ACTH concentration of 67 ng/l, and the midnight plasma cortisol concentration was raised at 580 nmol/l. In response to insulin induced hypoglycaemia the plasma cortisol concentration rose from 248 nmol/l to 483 nmol/l. An intravenous injection of 100 µg of corticotrophin releasing hormone-41 (CRF-41) produced a peak plasma concentration of ACTH of 107 ng/l after 15 minutes and a peak cortisol concentration of 1210 nmol/l after 60 minutes. An exaggerated response to CRF-41 is a recognised finding in pituitary-dependent Cushing's syndrome. The basal prolactin concentration was normal at 145 mU/l. Basal serum androgen concentrations were raised for a girl at her stage of puberty (dehydroepiandrosterone

Figure  Sagittal reconstruction of enhanced computed tomogram through the centre of pituitary fossa showing a large suprasellar lesion [arrow] extending into the hypothalamus.
cortisol, DHA [22.4 nmol/l, androstenedione 4.1 nmol/l, testosterone 2.4 nmol/l] but complete suppression of cortisol, DHA and androstenedione occurred after she was given 8 mg of dexamethasone orally each day for three days.

An abdominal ultrasound examination showed adrenal glands of normal size and morphology. A high resolution computed tomogram [GE9800] showed a suprasellar cystic lesion (figure). Following craniotomy this was resected, together with all residual pituitary tissue; histological examination confirmed a craniopharyngioma. There was no collection of basophilic cells suggestive of an adenoma, and no response to tumour tissue staining for ACTH, CRF, or bombesin. After operation her Cushingoid signs resolved rapidly and she required full pituitary replacement with thyroxine, hydrocortisone, growth hormone, oestrogen, and deamino-D-arginine vasopressin. During the year after the operation she grew 5 cm, and finally stopped growing at the age of 18. She has completed two years of follow up and has made an excellent recovery with no radiological evidence of residual tumour or biochemical recurrence of Cushing’s syndrome.

Discussion

This patient presented with loss of the normal harmony of growth and puberty, which usually indicates an endocrine abnormality. This allowed an early diagnosis of Cushing’s syndrome before florid signs of hypercortisolaemia became apparent. The diagnosis was confirmed by loss of the normal diurnal rhythm of cortisol secretion. The plasma ACTH concentration, dexamethasone suppression test, and response to intravenous CRF-41 differentiated Cushing’s disease from ectopic ACTH and primary adrenocortical hypersecretion. In addition, the histochemical studies of the tumour showed no evidence of ectopic hormone production. We can find no previously reported association between Cushing’s disease and craniopharyngioma. The possibility of hypersecretion of ACTH caused by pressure from a non-functioning hypothalamic-pituitary tumour has, however, been suggested. It is also possible that the hypersecretion may be due to release of inhibition rather than to direct stimulation.

There is controversy concerning the relative roles of the hypothalamus and the pituitary in the aetiology of Cushing’s disease. A primary role of the pituitary was unlikely in our patient as there was no histological evidence of a pituitary basophil adenoma. We suggest that hypothalamic dysfunction, caused by the craniopharyngioma, produced hypersecretion of ACTH secondary to increased secretion of CRF.

We thank Professor L. Rees, Department of Biochemical Endocrinology, St. Bartholomew’s Hospital, London, for the histochemical tumour studies.

References


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Received 11 March 1987