

Clinical Reports

Benign intracranial hypertension after pituitary surgery for Cushing's disease

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Summary: An 11 year old girl underwent successful transsphenoidal pituitary adenectomy for pituitary-dependent Cushing's syndrome. Three months after operation, just after stopping glucocorticoid replacement therapy, she developed benign intracranial hypertension. This resolved when exogenous glucocorticoids were restarted but occurred again when they were later stopped. On restarting glucocorticoids again, this second episode of intracranial hypertension resolved. This complication may have been due to the large fall in endogenous cortisol production after removal of her adenoma and subsequent persistent mild endogenous hypocortisolism.

Introduction

Pituitary-dependent Cushing's syndrome is rare in childhood. A questionnaire survey by the European Society for Paediatric Endocrinology in 1984 identified only 13 cases¹ and an American survey in 1977 involving 113 centres revealed 32 cases.² Until recently, bilateral adrenalectomy was the main surgical treatment in childhood but, because of the subsequent high incidence of Nelson's syndrome and need for lifelong glucocorticoid replacement therapy, pituitary surgery has become the preferred option. We report a case of benign intracranial hypertension developing in a young girl after transsphenoidal surgery for Cushing's disease.

Case report

An 11 year old girl was referred because of obesity and short stature. Since the age of 7 she had become increasingly obese and hirsute, and her height velocity had decreased. She was clinically Cushingoid, with plethora, truncal obesity, a buffalo hump, livid abdominal striae and hirsutism.

Twenty-four hour urinary free cortisol excretion, repeated on several occasions, was raised, up to 731 nmol in 24 hours (normal range 40–300

nmol/24 hours) and plasma adrenocorticotrophic hormone was inappropriately detectable at 26 ng/l. The urinary free cortisol excretion was suppressed by more than 50% during the high-dose dexamethasone suppression test. Computed tomographic (CT) and magnetic resonance (MRI) brain scans were normal, showing no pituitary abnormalities. Abdominal CT scan showed bilateral adrenal hyperplasia.

On the basis of these results, pituitary-dependent Cushing's syndrome was diagnosed. Adrenal blockade was achieved with metyrapone 250 mg four times daily. When urinary free cortisol excretion fell below 300 nmol in 24 hours, dexamethasone was started as glucocorticoid replacement therapy. Subsequently, a right transsphenoidal pituitary exploration was performed, at which adenomatous tissue was curetted from the pituitary fossa.

Postoperatively, hydrocortisone replacement therapy, 20 mg per day, was begun and subsequently slowly reduced. Because she was taking steroids, the patient was reviewed by an ophthalmologist one month after surgery and her optic fundi were noted to be normal. Her steroid medication ceased 12 weeks after operation. Two weeks later, she developed severe persistent headaches and nausea. On examination her Cushingoid appearance was noted to have dramatically resolved, but she had gross bilateral papilloedema, confirmed by an ophthalmologist and documented with retinal photographs. A CT brain scan was

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normal and in particular there was no evidence of venous sinus thrombosis. A lumbar puncture was declined.

In view of the normal CT brain scan, we considered that the papilloedema was due to benign intracranial hypertension. Dexamethasone was commenced at 2 mg per day and the headaches ceased, and after one month the papilloedema had resolved. Subsequently, the dexamethasone was reduced and stopped 3 months later. Soon after this, the headaches, early morning nausea and vomiting, and papilloedema returned. The dexamethasone was restarted and after a week the papilloedema and symptoms of raised intracranial pressure disappeared.

Endocrine investigations 8 months postoperatively showed normal thyroidal and gonadal axes, with a total thyroxine of 105 nmol/l (normal range 60–170), follicle stimulating hormone of 4.3 U/l (normal range 0.5–5) and luteinising hormone of 3.4 U/l (normal range 3–12). Measurement of 24-hour urinary free cortisol excretion revealed a degree of endogenous hypocortisolism, being on three successive occasions 44 nmol, 26 nmol and 44 nmol.

Presently she is well on a low dose of hydrocortisone, 2.5 mg daily, all features of Cushing's syndrome have been resolved, and the headaches and papilloedema have not recurred.

Discussion

Benign intracranial hypertension is a clinical syndrome comprising headache, visual disturbances and papilloedema, due to raised intracranial pressure, without focal neurology except that secondary to the intracranial hypertension. The cerebrospinal fluid (CSF) pressure is raised but its composition is normal. CT and MRI brain scans may sometimes show small lateral ventricles but are often normal.

It is a rare syndrome which is usually idiopathic, but with many known underlying causes and associations. It has been described in association with Addison's disease, Cushing's syndrome and

sudden changes in glucocorticoid levels such as after starting high-dose glucocorticoids or after sudden glucocorticoid withdrawal.

The pathophysiology is unknown except where there is a clear underlying cause (for example, decreased CSF reabsorption with cerebral venous sinus thrombosis), but postulated mechanisms include increased CSF formation,³ decreased reabsorption through arachnoid villi⁴ and increased brain volume.⁵ It can result in permanent visual loss.

It is possible that the large fall in endogenous glucocorticoid levels after surgery and subsequent persistent mild endogenous hypocortisolism in our patient caused the intracranial hypertension. This is supported by the resolution of the syndrome on starting dexamethasone, recurrence when this was stopped and further resolution when the dexamethasone was restarted.

An alternative cause could have been venous sinus thrombosis, which may occasionally complicate intracranial surgery but has not been reported after transsphenoidal pituitary procedures. There was no evidence of this on the CT brain scan and if this were the cause, it would not have been expected to respond to dexamethasone.

Benign intracranial hypertension as a complication of transsphenoidal pituitary adenectomy has been reported previously on three occasions, in a 7 year old girl,⁶ 17 year old man⁷ and a 29 year old woman.⁸ It has also been described in pituitary-dependent Cushing's syndrome following reduction of cortisol levels to normal by adrenal blockade with metyrapone and aminoglutethimide.⁹ Johnson *et al.* have reported decreased CSF reabsorption after acute withdrawal of exogenous glucocorticoids in dogs¹⁰ and a similar mechanism may occur in man.

Benign intracranial hypertension appears to be an uncommon complication of pituitary surgery for Cushing's disease and may be due to the fall in endogenous glucocorticoid levels and associated with subsequent endogenous hypocortisolism. Prompt recognition and treatment, initially by starting, or increasing the dose of, glucocorticoid replacement therapy, is important to prevent permanent visual loss.

References

1. Korth-Schutz, S. Cushing's syndrome and adrenocortical carcinoma in childhood. In: New, M.I. & Levin, L.S. (eds). *Pediatric and Adolescent Endocrinology*, Vol. 13: *Adrenal Diseases in Childhood*. Karger, New York, 1984, p. 185.
2. Hopwood, N.J. & Kenny, F.M. Incidence of Nelson's syndrome after adrenalectomy for Cushing's disease in children. *Am J Dis Child* 1977, **131**: 1353–1356.
3. Fishman, R.A. The pathophysiology of pseudotumor cerebri. *Arch Neurol* 1984, **41**: 257–258.
4. Sklar, F.H., Beyer, C.W., Jr, Ramanathan, M., Cooper, P.R. & Clark, W.K. Cerebrospinal fluid dynamics in patients with pseudotumor cerebri. *Neurosurgery* 1979, **5**: 208–216.
5. Raichle, M.E., Grubb, R.L., Phelps, M.E. *et al.* Cerebral haemodynamics and metabolism in pseudotumor cerebri. *Ann Neurol* 1978, **4**: 104–111.
6. Weissman, M.N., Page, L.K. & Bejar, R.L. Cushing's disease in childhood: benign intracranial hypertension after transsphenoidal adenectomy. *Neurosurgery* 1983, **13**: 195–198.

7. Fischer, E.G. & Anast, C.S. Letter to the Editor. *Neurosurgery* 1982, **10**: 297.
8. Martin, N.A., Linfoot, J. & Wilson, C.B. Development of pseudotumor cerebri after the removal of an adrenocorticotrophic hormone secreting pituitary adenoma: case report. *Neurosurgery* 1981, **8**: 699–702.
9. Newman, P.K., Snow, M. & Hudgson, P. Benign intracranial hypertension and Cushing's disease. *Br Med J* 1980, **281**: 113.
10. Johnson, I., Gilday, D.L. & Hendrick, E.B. Experimental effects of steroids and steroid withdrawal on cerebrospinal fluid absorption. *J Neurosurg* 1975, **42**: 690–695.