Is “benign intracranial hypertension” really benign?

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SUMMARY Hypothalamic-hypophyseal insufficiency has been found in seven of eight patients with so-called benign intracranial hypertension, of whom four showed an inadequate adrenal response to stress. The syndrome of benign intracranial hypertension cannot therefore be considered entirely benign and patients should receive full endocrinological assessment and follow up.

The development of sensitive and specific tests of hypothalamic and pituitary function has enabled the mechanisms of pituitary infarction to be re-examined. The ability to monitor intracranial pressures led to the detection of bursts of intracranial hypertension in “normal pressure” hydrocephalus which have been implicated as the cause of hypothalamic hypophyseal damage in such patients. Since the intracranial pressure in patients with the syndrome of benign intracranial hypertension may be severe enough to cause blindness in addition to papilloedema, we decided to assess the endocrine status of such patients.

Patients, Materials and Methods

Nine patients aged 24–55 years (mean 41·9 years) were diagnosed as having benign intracranial hypertension on the basis of history, physical examination, and the absence of demonstrable pathology to explain the raised intracranial pressure. One patient was male and the others female. Anterior pituitary function was assessed in response to insulin-induced hypoglycaemia, thyrotrophin-releasing hormone (TRH), and gonadotrophin-releasing hormone (GnRH) after an overnight fast. Basal samples were taken for routine blood count, biochemical profile, thyroxine, T3 uptake test, and either oestriadiol or total androgen (depending on the sex of the patient). All hormone assays were performed subject to the quality control criteria of the supraregional assay service, using methods described elsewhere. Blood sugar estimations were performed by the ferricyanide method of Technicon. All blood samples were taken via an indwelling forearm venous cannula. In the absence of suggestive symptoms, posterior pituitary function was not tested.

Results

Basal thyroid function (thyroxine and T3 uptake) tests were normal in all patients. The results of other endocrine tests are shown in the table. Only two patients (cases 2 and 6) had received steroids at any time and in the former they had not been given for six months before testing. The latter patient was on dexamethasone at the time of testing and this probably explains the blunted, sustained TSH response to TRH.

The cortisol response to insulin-induced hypoglycaemia was abnormal in five patients (cases 1, 4, 7, 8, and 9) and was not measured in the patient receiving dexamethasone. Although the basal resting cortisol levels were within normal limits, the response to stress was inadequate. All patients experienced definite symptoms of hypoglycaemia (see table). Growth hormone responses to the same hypoglycaemic stimulus were abnormal in five patients (cases 2, 4, 6, 7, and 8) although a rise from undetectable levels to 18 mU/l in case 6 probably represented “normal” function for a patient receiving steroids.

The luteinising hormone (LH) response to GnRH was abnormally sustained in three patients.
Table  Results of anterior pituitary function testing

<table>
<thead>
<tr>
<th>Case No</th>
<th>Sex</th>
<th>Age (yrs)</th>
<th>TSH (mU/l)</th>
<th>LH (U/l)</th>
<th>FSH (U/l)</th>
<th>Total androgen (nmol/l)</th>
<th>Oestradiol (pmol/l)</th>
<th>Cortisol (nmol/l)</th>
<th>Growth hormone (mU/l)</th>
<th>Pro-lactin (mU/l)</th>
<th>Minimum blood sugar (mmol/l)</th>
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<td>26</td>
<td>8</td>
<td>33</td>
<td>26</td>
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<td>Insufficient</td>
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<td>610</td>
<td>560</td>
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<td>2 7 5</td>
<td>3</td>
<td>280 400</td>
<td>510</td>
<td>450</td>
<td>1 2 42</td>
</tr>
</tbody>
</table>

Normal value: 1.7 5-21 30

*Male.
†Female (at any stage of cycle).
‡Post-menopausal females.

Reference standards for TSH, LH, FSH, prolactin, and growth hormone assays were MRC 68/38, MRC 69/104, MRC 71/222, and MRC 66/217 respectively.

Discussion

Benign intracranial hypertension pseudotumour cerebri occurs mainly in young women, and is characterized by pseudotumour cerebri with papilloedema and optic atrophy, as well as by the presence of raised intracranial pressure, delayed venous drainage, and abnormal endocrine function. Our results show that when steroid dosage is increased, both hypothalamic hormone levels and serum prolactin levels rise, and that this is associated with increased intracranial pressure for which the patient is subject to gradual rise in intracranial pressure caused by uncontrolled intracranial pressure caused by uncontrolled intracranial pressure. This may be associated with the development of an adrenocortical response to stress and is sometimes accompanied by the development of a pseudo-tumour cerebri. The diagnosis of an adrenocortical response to stress is usually made by the demonstration of increased intracranial pressure for which the patient is subject to gradual rise in intracranial pressure caused by uncontrolled intracranial pressure.
cranial hypertension may be caused by hypothalamic damage leading to inadequate production of prolactin-release-inhibiting factor.

The difficulties in interpreting the results in patients receiving steroids are exemplified in case 6, where the TSH and growth hormone responses may have been due either to the steroids or to local damage, and the ACTH-adrenal response to stress could not be tested. In the light of the other results, patients such as these need reassessing after cautious withdrawal of steroids, and replacement therapy with steroids should be given for trauma or illness pending such reassessment.

So-called benign intracranial hypertension may not be completely benign and patients with this diagnosis should be assessed and followed up endocrinologically. Assessment should be performed after cessation of steroid therapy if this has been given, and if patients have an inadequate cortisol response to stress, replacement therapy should be started, as for other patients with adrenal insufficiency.

We thank the various physicians, neurologists and neurosurgeons who allowed us to examine their patients; Professor Butt, Midland Endocrine Laboratory, Women's Hospital, Birmingham, and Dr Northam, General Hospital, Birmingham, for endocrine and biochemical estimations; Hoechst Pharmaceuticals, who supplied the gonadotrophin-releasing hormone; and, of course, the patients.

References


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