CASE REPORT

Pituitary insufficiency and regression of acromegaly caused by pituitary apoplexy following cerebral angiography

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Pituitary apoplexy is an acute clinical syndrome characterized by visual defects, ophthalmoplegia (1) and a depressed sensorium (2, 3). It is caused by acute compression of the perisellar structures or by meningeal irritation. This results from the enlargement of the pituitary gland by infarction or haemorrhage. In most instances it occurs in a pre-existing pituitary adenoma, which until then frequently had been clinically silent (4–7). Ischaemic or haemorrhagic necrosis of a pituitary adenoma may be entirely asymptomatic. It may lead to improvement of a pre-existing pathological condition, like spontaneous cure of an anterior pituitary hormone hypersecretory state, or a dramatic regression in pituitary tumour size (4–11). Furthermore, haemorrhage of the non-tumour-bearing pituitary gland may occur in association with specific clinical conditions like external radiation therapy, bleeding disorders, abrupt changes in the intra-arterial or intracranial pressure and post-partum haemorrhage. The latter situation resulting in pituitary necrosis is also known as Sheehan’s syndrome (12). Furthermore, several medications have been associated with pituitary apoplexy: anticoagulants (13), bromocriptine (14, 15), pituitary stimulation tests (16–20) and GnRH-agonists (21). In all these cases, the clinical signs of pituitary enlargement may not become clinically manifest, as these conditions are mostly limited to the normal pituitary boundaries, preventing compression of the perisellar structures (4–7).

We present a patient with clinically active acromegaly caused by a growth hormone (GH)-secreting pituitary macroadenoma. He developed pituitary apoplexy following pre-operative angiography of the cerebral blood vessels. This resulted in a significant regression of the pituitary tumour size, clinical cure of acromegaly and anterior and posterior pituitary insufficiency.

Case report

A 32-year-old male presented with progressive enlargement of the hands and coarsening of his facial features. He had noted easy fatigueability, excessive perspiration, clumsiness and habitual snoring which had developed over a period of approximately 4 years. Visual defects had not been noticed. There were no complaints of paraesthesias. The medical history was negative for cardiovascular or neurological diseases. There was no diabetes mellitus. On physical examination typical acromegalic features were present. The systemic blood pressure was 130/80 mmHg and peripheral arterial pulsations were normal. Visual field examination showed no defects. The ocular movements were normal. On admission, laboratory results showed an elevated IGF-I level of 119.8 nmol/l (N < 45 nmol/l; Table 1). The IGF binding protein 3 (IGFBP-3) level was 4.8 mg/l (N: 2.1–4.8 mg/l; Table 1). The mean GH level, which was calculated from GH levels in 18 serum samples taken over a period of 24 h, amounted to 140.3 μg/l (N < 2.0 μg/l; Table 1). Basal plasma cortisol, testosterone, prolactin levels and 24 h cortisoluria were within normal limits (Table 1). Total and free thyroxine levels were reduced (Table 1) and thyroxine therapy was instituted. There was no diabetes insipidus. Blood glucose levels ranged from 3.7 to 5.9 mmol/l, and...
Table 1. Endocrine parameters before and after angiography.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before angiography</th>
<th>Immediately after angiography</th>
<th>3.5 Months after angiography</th>
<th>Normal values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean GH</td>
<td>140.3</td>
<td>0.3</td>
<td>&lt; 2.0 µg/l</td>
<td></td>
</tr>
<tr>
<td>IGF-I</td>
<td>119.8</td>
<td>44.4</td>
<td>&lt; 45 nmol/l</td>
<td></td>
</tr>
<tr>
<td>IGFBP-3</td>
<td>4.8</td>
<td>2.0</td>
<td>2.1–4.8 mg/l</td>
<td></td>
</tr>
<tr>
<td>PRL</td>
<td>11.6</td>
<td>0.9</td>
<td>&lt; 12 µg/l</td>
<td></td>
</tr>
<tr>
<td>LH</td>
<td>1.0</td>
<td>1.8</td>
<td>1 µ/l</td>
<td></td>
</tr>
<tr>
<td>FSH</td>
<td>2.5</td>
<td>2.6</td>
<td>1–7 µg/l</td>
<td></td>
</tr>
<tr>
<td>Testosterone</td>
<td>11.2</td>
<td>6.3</td>
<td>10–30 nmol/l</td>
<td></td>
</tr>
<tr>
<td>TSH</td>
<td>0.58</td>
<td>0.33*</td>
<td>0.2–4.2 mU/l</td>
<td></td>
</tr>
<tr>
<td>Free T₄</td>
<td>7.3</td>
<td>14.9*</td>
<td>11–25 pmol/l</td>
<td></td>
</tr>
<tr>
<td>Total T₄</td>
<td>54.0</td>
<td>91.0*</td>
<td>64–132 nmol/l</td>
<td></td>
</tr>
<tr>
<td>Cortisol</td>
<td>432.0</td>
<td>17</td>
<td>&gt; 140 nmol/l</td>
<td></td>
</tr>
</tbody>
</table>

*Under replacement therapy with L-thyroxine.

the glycosylated haemoglobin level amounted to 5.6% (N = 5.0–6.3%). A TRH test showed a paradoxical rise in serum GH, and T₄-weighted magnetic resonance images obtained in the coronal plane showed a pituitary macroadenoma of 24 × 22 mm, with slight suprasellar expansion (Fig. 1A). A preoperative angiogram performed according to the Seldinger method showed normal pituitary vasculature and no aneurysms. He routinely received an intramuscular injection with 100 mg of hydrocortisone 30 min prior to angiography. Seven hours after the angiographic procedure, the patient developed headache, nausea and vomiting. At physical examination he appeared to be in discomfort, because of severe headache and a decreased sensorium. However, no visual disturbances or ophthalmoplegia had developed. Blood pressure remained stable. Acute secondary adrenal failure due to pituitary apoplexy was suspected. A blood sample was taken for plasma cortisol measurement and treatment with corticosteroids was instituted. Thereafter, symptomatology improved dramatically. The plasma cortisol level at the time of the maximal clinical distress amounted only to 17 nmol/l (0.5 µg/dl). In view of this very low cortisol level it was decided not to carry out a pituitary-adrenal axis functional test. Shortly after the start of cortisol administration, the patient developed central diabetes insipidus. He was eventually discharged on replacement therapy with hydrocortisone, L-thyroxine and desmopressin.

Three and a half months later the patient was readmitted for clinical re-evaluation. There had been a dramatic regression of the acromegalic features. The plasma GH levels had returned to the normal range, with a mean 24 h GH level of 0.3 µg/l. A TRH test was

![Fig. 1. The T₁-weighted pituitary magnetic resonance images in the coronal plane after administration of Gd-DTPA in a 32-year-old patient with acromegaly before (A) and 3.5 months after (B) angiography and pituitary apoplexy. Note the significant reduction in pituitary tumour volume.](image-url)
repeated, showing a basal GH level of 0.4 μg/l, which reduced to 0.2 μg/l 60 min after TRH stimulation. The IGF-I level was within normal limits (44.4 nmol/l; Table 1) and the IGFBP-3 level was 2.0 mg/l (Table 1). The plasma testosterone level was 6.3 nmol/l (N = 10–30; Table 1). Replacement therapy with testosterone undecanoate was instituted. T2-weighted magnetic resonance images obtained in the coronal plane showed a significant reduction in the size of the pituitary macroadenoma, which now measured 15 × 14 mm. Furthermore, the suprasellar expansion of the tumour had disappeared (Fig. 1B).

Discussion

It is well known that pituitary tumours are particularly prone to haemorrhage and necrosis (4–6). One theory suggests that this is caused by the tumour outstripping its blood supply (4, 5). However, pituitary apoplexy may also develop in microadenomas or in normal pituitaries (2). Another theory suggests that pituitary tumour growth causes compression of the superior hypophyseal artery against the sellar diaphragm, thereby inducing ischaemia (4, 5). However, if pituitary adenomas are supplied by blood from the inferior hypophyseal artery, like the posterior pituitary, interference with the superior hypophyseal arterial blood supply may lead to ischaemia of the anterior pituitary rather than of the adenoma. In general, sudden changes in the arterial pressure occurring during cerebral angiography may also result in apoplexy (4, 5). Limited information exists concerning pituitary haemorrhage or infarction occurring in connection with cerebral angiography (22). In general, neurological complications of cerebral angiography in patients bearing tumours of the central nervous system only occur in approximately 1% of cases (23).

The sudden onset of severe headache is the most prominent symptom of pituitary apoplexy. In the majority of cases also visual disturbances develop. Frequently, clinical signs of meningeal irritation with a depressed sensorium, nausea and vomiting develop. Cranial nerve palsies of nerves III, IV and VI may develop (2–5). Anterior and posterior pituitary insufficiencies may develop, which sometimes go unnoticed, and life-threatening secondary adrenal insufficiency may ensue. Following pituitary apoplexy, GH deficiency has been reported in 88–100%, gonadotrophin deficiency in 58–76%, ACTH deficiency in 66–75% and TSH deficiency in 42–50% of patients. Transient or persistent diabetes insipidus develops in 4% and 2% of the patients, respectively (3, 24).


The pituitary tumours of approximately 9.5–16.6% of patients undergoing elective pituitary surgery show evidence of haemorrhagic or necrotic degradation. Only a minority of these patients had presented with a clinical history of an acute episode, which was suggestive for pituitary apoplexy. Patients with GH-secreting adenomas do not seem to be more prone to pituitary apoplexy than patients harbouring other pituitary adenomas (6, 7).

In the present case, we describe pituitary apoplexy developing following cerebral angiography. The patient routinely received hydrocortisone (100 mg) 30 min prior to angiography. Jordan et al. have described a patient with Nelson’s syndrome who developed pituitary apoplexy following high-dose dexamethasone testing (25). Therefore, a direct causative role of corticosteroids in the induction of apoplexy in our patient cannot be excluded. Seven hours after the angiographic procedure, pituitary apoplexy was suspected because of complaints of headache, nausea and vomiting together with a decreased sensorium. No visual disturbances or ophthalmoplegia developed. Apart from normalization of the 24 h GH profile and IGF-I and IGFBP-3 levels, anterior and posterior pituitary insufficiency developed over a period of 3.5 months. However, to date we cannot exclude that regrowth of the pituitary tumour or recurrence of symptoms of acromegaly may develop in future, thereby necessitating adjuvant therapy. Whether apoplexy was caused by infarction or haemorrhage is not clear. Regrettfully, no immediate neuroradiological imaging and/or anterior pituitary function testing was carried out when clinical symptomatology developed. With the use of T2-weighted magnetic resonance images obtained in the acute phase one can easily differentiate between the hyperintense signal caused by pituitary infarction and the hypointense signal of an acute haemorrhage (26, 27).

Immediate neurosurgical intervention for pituitary apoplexy is often required when severe symptoms caused by tumour expansion have developed (2, 4, 5). In selected cases, conservative management with corticosteroids may also produce satisfactory results (28). In the case reported here, there was no longer an indication for neurosurgical treatment, as the pituitary apoplexy did not result in tumour expansion, whereas the signs and symptoms of GH excess disappeared.

In conclusion, asymptomatic pituitary haemorrhage and infarction frequently occur, but acute symptomatic pituitary apoplexy, which often requires immediate medical and/or neurosurgical intervention, is particularly rare. In patients with a known pituitary adenoma, who acutely develop severe headaches, visual disturbances, ophthalmoplegia or major neurological defects in combination with nausea and vomiting, this diagnosis should be considered. Consequently, neuroradiological investigation should be performed acutely and corticosteroids instituted immediately (after blood samples for hormonal estimation have been taken).
References

19. Korsic M. Pituitary apoplexy following the administration of gonadotrophin releasing hormone. Clin Endocrinol (Oxf) 1994;41:696-7

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