Spontaneous pituitary necrosis

Spontaneous pituitary necrosis follows a variable clinical course. Three different clinical presentations are reported.

Case 1
A 44-year-old woman with amenorrhoeal features and 27 years' amenorrhoea presented in coma which had been preceded by severe headache. She had pale nipples, fever (38°C), signs of meningial irritation, and no pubic or axillary hair. The fundus and visual fields were normal. The cerebrospinal fluid (CSF) was under increased pressure and contained 0·5 g/l of protein and 0·02 x 10⁶ lymphocytes/l (20 mm²). Her skull x-ray film showed an enlarged pituitary fossa, and spontaneous infarction of a pituitary tumour was diagnosed. Corticosteroid treatment rapidly improved her condition. Two years later endocrine assessment showed mild hypothyroidism (protein bound iodine (PBI) 240 nmol/l (3·1 µg/100 ml); normal 315-630 nmol/l (4·0-8·0 µg/100 ml) and low plasma 11-hydroxycorticosteroids (11-OHCS: 70 nmol/l (2·5 µg/100 ml) at 9 am; normal 190-720, p.m. and there were 6·9-26 µg/100 ml (normal)). A standard insulin tolerance test produced hypoglycaemia with a minimum blood sugar level of 1·1 mmol/l (20 mg/100 ml) when the maximum values of plasma 11-OHCS and growth hormone (GH) were below normal (88 nmol/l (3·2 µg/100 ml) and 10·5 µU/g respectively). GH levels were not suppressed during a standard glucose tolerance test (minimum GH level 82 µU/g), confirming autonomous GH production by the pituitary tumour. Serum luteinising hormone was 3·6 U/I and serum follicle stimulating hormone was 54 U/I, compared with normal postmenopausal levels of 20 U/I and 12·5 U/I respectively. The fundi and visual fields remained normal. L-thyroxine was combined with cortisone therapy and regular follow-up was maintained. Seven years later bitemporal hemianopia had developed with further enlargement of the pituitary fossa and irregular destruction of the floor and anterior wall. A huge intrasellar tumour containing fresh bloodstaining the optic nerves was removed. Histology showed a pituitary adenoma containing predominantly chromophobe cells with 15-20% acidophilic cells. Postoperative irradiation was given to avoid recurrence. She is currently well on replacement therapy and her visual fields have improved since surgery.

Case 2
A 26-year-old woman presented with amenorrhoea and galactorrhoea after oral contraceptive therapy. Skull x-ray films showed an enlarged pituitary fossa, and air encephalography (AEG) was performed to delineate the extent of the tumour. Thirty minutes after AEG she developed a severe headache, neck rigidity, and hypotension. The CSF protein content was 0·9 g/l with 0·13 - 10³ lymphocytes/l (130 mm³). She recovered well on parenteral corticosteroids. Results of endocrine assessment performed two months after AEG showed that the adrenocortical response to hypoglycaemia had disappeared and the GH response remained impaired (table). Cortisol therapy was prescribed and she is currently well though her periods have not restarted.

Insulin tolerance test results in case 2 before and after air encephalography (AEG). Clinical hypoglycaemia was achieved in both tests. Values in brackets obtained after AEG

<table>
<thead>
<tr>
<th>Time (min):</th>
<th>0</th>
<th>30</th>
<th>60</th>
<th>90</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood sugar (mmol/l)</td>
<td>4·0 (3·9)</td>
<td>3·4 (3·7)</td>
<td>3·8 (5·0)</td>
<td></td>
</tr>
<tr>
<td>Plasma 11-OHCS (nmol/l)</td>
<td>270 (270)</td>
<td>490 (360)</td>
<td>400 (300)</td>
<td></td>
</tr>
<tr>
<td>Serum GH (µg/l)</td>
<td>3·8 (3·5)</td>
<td>6·1 (1·9)</td>
<td>5·1 (1·4)</td>
<td></td>
</tr>
</tbody>
</table>

Conversion: SI to traditional units—Glucose: 1 mmol/l = 18 mg/100 ml. 11-OHCS: 1 nmol/l = 0·363 µg/100 ml.

Case 3
A 69-year-old man reported persistent headache. Two days later he was admitted in coma with fever (39°C), neck rigidity, right oculomotor nerve palsy, and right hemiplegia. Skull x-ray films showed an enlarged pituitary fossa. The CSF was xanthochromic with many red and white cells; the protein content was increased to 2·5 g/l. An intracerebral haemorrhage was diagnosed and treated. He was discharged after a few days. Two years later he presented with progressive lethargy, drowsiness, confusion, and hypotension. PBI was 250 nmol/l (3·2 µg/100 ml), Thytopac-3 126 (normal 92-117), and 9 am plasma 11-OHCS 80 nmol/l (2·9 µg/100 ml). Investigations confirmed that he had developed pituitary failure. He is currently well on L-thyroxine and cortisol replacement therapy.

Discussion
The basic pathology of spontaneous haemorrhage into a pituitary tumour is unclear; it may be due to rapid enlargement of the adenoma with infarction or rupture of the fine-walled vessels in the tumour. There is rarely enough tissue left to maintain normal function. We are unaware of reports of further growth of a pituitary tumour after apparent infarction sufficient to cause compression of the visual pathways as seen in case 1. The visual fields and skull x-ray picture should obviously be checked periodically after spontaneous infarction of a pituitary tumour. Pituitary infarction precipitated by AEG is rare but has been reported in a patient with acromegaly.

Spontaneous pituitary necrosis is more common although it is of interest that the clinical features of hypopituitarism in the third patient were not apparent for two years.

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Rapid clonidine withdrawal with blood pressure overshoot exaggerated by beta-blockade

A disconcerting problem in treating hypertension with clonidine is the possibility of a severe rebound rise in blood pressure if the drug is stopped abruptly. The reaction may resemble the crisis seen in patients with a phaeochromocytoma. The combination of a beta-adrenoceptor blocker with one of the vasodilator group of antihypertensive drugs (hydrallazine, prazosin, clonidine) has become popular. Since beta-blocking drugs increase peripheral vascular resistance, theoretically a hypertensive crisis after a rapid withdrawal of clonidine could be aggravated in a patient who was also taking a beta-blocker. We report a case in which the patient started taking timolol and at the same time suddenly discontinued clonidine, and subsequently suffered a devastating blood pressure rebound.

Case report
A 60-year-old woman with a 10-month history of rapidly progressive glomerulonephritis and complicating hypertension was receiving prednisone 15 mg/day, warfarin 2 mg/day, and clonidine 0·15 mg eight-hourly. When seen for assessment she was well but her blood pressure was 180/140 mm Hg, her renal arteries were narrowed, and there were moderate arteriogenous crossing changes. The blood urea was 14·9 mmol/l (90 mg/100 ml) and the serum creatinine 180 µmol/l (2·1 mg/100 ml).

The beta-adrenoceptor blocking drug timolol 5 mg daily was added to the patient's antihypertensive regimen. In error, she immediately discontinued the clonidine. Forty-eight hours later she developed a throbbing frontal headache, mild confusion, and profound lethargy. Over the next 24 hours the headache became excruciating, the confusion more marked, she developed

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