Short report

Apoplexy in small pituitary tumours

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SUMMARY Three cases are described in which the typical clinical features of pituitary apoplexy were associated with a normal pituitary fossa on plain skull radiographs. Failure to consider pituitary disease led to considerable delay in the diagnosis of two of the three patients. Catastrophic haemorrhage may occur even in small pituitary tumours and may result in the clinical syndrome of apoplexy with or without subsequent hypopituitarism.

The clinical syndrome of pituitary apoplexy was first described in 1905.¹ It results from haemorrhage into or infarction of a pituitary tumour and is characterised by sudden severe headache, vomiting, photophobia, prostration, cranial nerve compression and subsequent hypopituitarism, although none of these features is invariable.² In recent published series a history of such an apoplectic attack of greater or less severity was obtained in 10.0% of 586, 9.1% of 560, 5.6% of 320 and 6.0% of 100 cases of pituitary tumour who came to surgery.³⁻⁶ In these series an approximately equal number of patients had evidence of asymptomatic haemorrhage into the tumour. If endocrine disease is clinically overt or if the pituitary fossa is grossly expanded on plain skull radiographs, the diagnosis of acute pituitary apoplexy may present little difficulty. However, we have recently encountered three patients in whom there was no clinical suspicion of endocrine disease; the pituitary fossa was normal in each case.

Case reports

Case 1 A 63-year-old housewife was in good health until she collapsed suddenly at her granddaughter's wedding in April 1981. She was taking metoprolol for hypertension, but no other medication. She was drowsy and vomited repeatedly through the succeeding night, but she had no headache. Her condition settled over two days but she remained vaguely unwell, and lost weight. She was admitted to hospital three times before the diagnosis of hypopituitarism was

made, 3 months after the initial collapse. The clinical diagnosis was confirmed biochemically: basal plasma cortisol was 82 and 47 nmol/l (rising after Synacthen, but not after hypoglycaemia); free thyroxine was 5 pmol/l (normal 9.5-24) with low TSH (2.9 mU/l); LH (0.4 U/l) and FSH (0.5 U/l) were low for a post-menopausal woman; basal GH was <1 mU/l (no response to hypoglycaemia); basal prolactin was 650, 570 and 730 mU/l (reference range 100-700 mU/l). She recovered completely when treated with hydrocortisone and thyroxine. Plain skull radiographs were reported normal, as were visual fields. High resolution CT scan performed in 1983 demonstrated a pituitary adenoma with suprasellar extension reaching to the chiasm, with a low-density centre compatible with central infarction.

Case 2 A 36-year-old male company director was well until 1981 when he had two grand mal epileptic fits. He was treated with valproate 800 mg daily, and had no further attacks. On the afternoon of 28 March 1983 he suddenly felt unwell, with faintness, sweating and weak legs. Headache was initially mild but worsened over a period of hours. He went to bed and vomited repeatedly through the night. His sleep was disturbed also by vivid nightmares. By the next morning he noted a drooping eyelid and double vision. He was admitted to hospital and subsequently transferred to a neurosurgical centre. There were signs of a complete right third nerve palsy but the IV, V and VI nerves were spared. Visual acuity and visual fields were normal. Plain skull radiographs, CT scan (first generation), CSF examination, carotid angiography and orbital venography were unhelpful. His third nerve palsy improved spontaneously and he was discharged from hospital without treatment. After discharge he had persistent malaise, with weakness and dizziness, and he walked with a stick. During the succeeding four months he noticed loss of libido, and decreasing beard growth. Hypopituitarism was suspected by his general physician and confirmed after admission to hospital. At this time he had no residual neurological deficit; visual fields remained full. Basal 9 am cortisol was 171 nmol/l (rising to only 406 fol-

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Received 12 December 1985.
Accepted 25 January 1986.

lowing symptomatic hypoglycaemia; glucose nadir 2.2 mmol/l). Serum free thyroxine was 4.2 pmol/l, and TSH was inappropriately low. Testosterone was not measured. Basal LH was 2 U/l and rose to 5 U/l after 100 µg IV LHRH (FSH 2 U/l, showed no rise). Serum prolactin was 120 mU/l and GH remained undetectable through the hypoglycaemia stress test. On replacement therapy with hydrocortisone, thyroxine and testosterone he is symptom-free. High resolution CT scan performed in February 1984 showed evidence of a small intrasellar adenoma with a low density area breaching the dura on the medial wall of the right cavernous sinus, compatible with previous apoplexy with blood and/or infarcted adenoma reaching laterally to compress the right third nerve.

Case 3 An obese 30-year-old secretary was admitted to hospital as an emergency in October 1984 with severe, central frontal headache which had started abruptly two weeks earlier, waking her from sleep. Apart from appendicitis 6 years before she had been in good health and was taking only the contraceptive pill, Norimin (ethinylloestradiol and norethisterone). The headache was associated with photophobia and was worse on waking or with coughing. On examination she had bitemporal visual field loss but no other clinical or neurological signs. Plain skull radiographs were normal as were all biochemical investigations. CT scan (first generation, October 1984) was unhelpful, but high resolution CT scan in the convalescent phase (March 1985) revealed a small pituitary gland with a low density area in its upper part. By March 1985 her visual fields had largely recovered and her corrected visual acuity was normal.

Discussion

The factors which may precipitate haemorrhage into or infarction of pituitary adenomas are unknown, although in rare cases the administration of TRH, anti-coagulants and other drugs, trauma, carotid angiography, preceding radiotherapy and diabetic ketoacidosis have been implicated.² Although different authors have found that age of the patient⁴ or endocrinological activity of the tumour³ was important, in most cases it is assumed that apoplexy results from ischaemic necrosis related to the particular vascular disposition of the neoplasm. Each of the recent large series or reviews has emphasised that there may be no preceding suspicion of pituitary disease in patients who present with acute apoplexy. Moreover the character of the attack varies widely and there may be no neurological signs to indicate the site of the vascular accident; some may present as acute subarachnoid haemorrhage. Thus a plain skull radiograph should always be obtained in such cases. In published series the sella was abnormal in all of 10⁶, 58⁵ and 72³ cases;

in a review of other published papers Fitzpatrick reported an abnormal fossa in 52 out of 56.⁷

Each of these recent reports has drawn attention also to the poor prognosis, with apoplexy being considered fatal "in most cases"² and "if not treated early".⁵ Most have recommended "prompt surgical intervention as the treatment of choice".⁶ However these views are based on experience gained in neurosurgical units and may be critically influenced by referral patterns. In our own general medical practice we have encountered three cases of acute apoplexy in patients with no preexisting knowledge of pituitary disease in three years. The skull radiograph of each was subsequently reviewed independently by two consultant radiologists and judged normal. It should be noted that the initial CT scan (first generation) was also normal in both patients who had it done. In general the nature of the attack in these three patients may have been milder, and although surgical intervention would have been considered if the diagnosis had been established in the acute phase, each recovered with conservative management.

We thank Professor AE Tattersfield for referring one of these patients, and Dr B Kendall, Dr M Charlesworth (Cases 1 and 2) and Dr I Holland (Case 3) for reporting on the high resolution CT scans. We thank Sue Saunders for preparing the manuscript.

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