Simultaneous occurrence of transient resolving thyrotoxicosis due to painless thyroiditis, hypopituitarism and diabetes insipidus following pituitary apoplexy

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Summary: A rare case of concomitant association of transient thyrotoxicosis due to painless thyroiditis, hypopituitarism and central diabetes insipidus following spontaneous pituitary apoplexy is presented.

Introduction

Pituitary apoplexy is characterized by a wide spectrum of clinical features, not only in mode of presentation but also in outcome.^{1–3} We treated a patient with a previously undiagnosed pituitary tumour in whom spontaneous pituitary apoplexy occurred. Subsequently, impairments of both anterior and posterior pituitary function and transient resolving thyrotoxicosis secondary to painless (silent) thyroiditis^{4,5} developed. To our knowledge, these events concomitant with pituitary apoplexy have not been previously reported.

Case report

A 61 year old post-menopausal Japanese housewife was admitted to Fukuoka University Hospital in May, 1986 with marked general malaise, polydipsia and weight loss which had become progressively worse during a 4-month period. She had experienced the abrupt onset of severe headache associated with nausea and blurring vision with diplopia. The visual disturbance and headache gradually improved but 3 weeks prior to admission she had a recurrent attack of headache and transient fever (38.5°C). Menarche was at age 15 years and the menopause at 45. Galactorrhea occurred on one occasion only at the age of 55. There was no personal or family history of thyroid or autoimmune disease. She had not ingested excessive amounts of iodine or thyroid hormone.

On admission, she was alert and oriented, but

distressed by marked general fatigue. Physical examinations revealed a fine tremor, dry skin and nervousness. She had no thyroid enlargement or tenderness, exophthalmos or galactorrhoea. Her blood pressure was 105/64 mmHg with variable sinus tachycardia (92–105 beats/min). Visual field perimetry was also intact. Routine laboratory studies were negative except for a low serum protein (51 g/l), hypocholesterolaemia (1.90–2.22 mmol/l), hypernatraemia (143–151 mmol/l) and low specific gravity of urine. Test for C-reactive protein was negative and the erythrocyte sedimentation rate was 12 mm/h.

An impairment in corticotrophin secretion was suspected from the low plasma cortisol (27.6 nmol/l at 08.00 h; normal 110–520 nmol/l) and the low urinary excretion of 17-hydroxycorticosteroids (1.1 mg/day; normal 1.9–6.1 mg/day) and 17-ketosteroids (0.6 mg/day; normal 3.1–8.8 mg/day), and an appropriate response to the rapid ACTH (Cortrosyn) test. Plasma ACTH and cortisol responses to ovine corticotrophin releasing hormone (ovine CRF: 100 µg, i.v.) also were diminished. Basal level of growth hormone (<0.3 µg/l; normal <5.0 µg/l), somatomedin C (0.14 U/ml; normal 0.3 to 3.0 U/ml) and gonadotrophin (LH 3.9 IU/l and FSH <1.9 IU/l) were also low, and responses to stimulation tests [Insulin-stress, L-dopa and luteinizing hormone releasing hormone (LH-RH)] were all blunted. Although an X-ray of the skull revealed no abnormalities, brain computed tomographic (CT) scan and magnetic resonance imaging (MRI) demonstrated a suprasellar mass that, after infusion, developed a peripheral ring-like enhancement⁶ and a large hyperintense pituitary mass,⁷ respectively (Figure 1a,b).

A diagnosis of pituitary apoplexy associated with anterior pituitary failure was made. However,

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Accepted: 2 July 1990

Figure 1 (a) Postcontrast computerized tomogram (transverse and coronal). Ring-like peripheral enhancement of suprasellar extension of the tumour (arrow) is the necrotic pituitary tissue (June 1986). (b) Sagittal and coronal T1-weighted magnetic resonance imaging (MRI) scans showed increased signal intra- and suprasellar pituitary tumour. Inset: coronal section showing elevation of the optic chiasma (June 1986). (c) T1-weighted MRI showing spontaneous reduction of the intra- and suprasellar pituitary mass after 1 year (June 1987).

the initial levels of thyroid hormones were elevated, as follows: total thyroxine (T4) 212.4 nmol/l (normal 59.2 to 157.0 nmol/l), free triiodothyronine (T3) 7.6 pg/ml (normal 3.0 to 5.8 pg/ml), free T4 42.5 pmol/l (normal 10.9 to 28.9 pmol/l), T3 resin uptake 0.41 litres (normal 0.23 to 0.35 litres) and suppressed thyroid stimulating hormone (TSH) to less than 0.3 mU/l (normal 0.30 to 4.0 mU/l). TSH responses to thyrotrophin releasing hormone (TRH: 500 µg, i.v.) were all suppressed (all < 1.3 mU/l). Basal prolactin (PRL) was slightly elevated (120–150 µg/l; normal < 30 µg/l) and the response to TRH was adequate (peak 260 µg/l at 60 min). The anti-TSH receptor antibody (measured by thyrotrophin binding inhibiting immunoglobulin: TBII) was –6.9% (normal < ± 10%) and anti-pituitary antibodies (indirect immunofluorescence technique using rat pituitary GH3 cell and mouse pituitary AtT20 cell as the antigen)⁸ were negative. Both anti-thyroglobulin antibody (TGHA) and anti-microsomal antibody (MCHA) (haemagglutination assay) were repeatedly positive at the titres 1:200 to 1:400 and 1:800 to 1:2,560 (normal, both < 1:100), respectively. A thyroid scan with ^{99m}Tc revealed no uptake in the thyroid area.

These findings led to the diagnosis of 'painless (silent) thyroiditis' with thyrotoxicosis.^{4,5} Within 3 weeks, she was biochemically euthyroid, while on no medication (free T3 3.7 pg/ml and free T4 21.4 pmol/l). Four weeks later, the thyroid hormone levels markedly fell to severe hypothyroid ranges (free T3 1.8 pg/ml, free T4 8.1 pmol/l and TSH < 1.3 mU/l). At that time repeated radioactive ^{99m}Tc uptake had risen despite a low uptake. Before replacement, the 24-h ¹²³I uptake was 33.7% (normal 10 to 40%). Repeated TRH stimulation resulted in a delayed response in plasma TSH, as noted in hypothalamic disorders⁹ (basal 5.1 mU/l and peak TSH 17.0 mU/l at 90 min). Hydrocortisone (25 mg/day) and subsequent L-thyroxine (50–100 µg/day) were given, with marked improvement in the general clinical condition.

When hydrocortisone was substituted, daily urine output abruptly increased to about 8 to 9 litres with low osmolality (less than 200 mmol/kg) and diabetes insipidus was suspected (so-called masked diabetes insipidus due to rapid development of hypopituitarism).² After water deprivation for 8 h, plasma osmolality rose to 291 mmol/kg, but the urine osmolality remained low (231 mmol/

kg). Plasma antidiuretic hormones (ADH) were not elevated (all < 1.0 pg/dl; normal < 7.5 pg/dl). With the administration of 5.0 U of pitressin, the urine osmolality rapidly increased (490 mmol/kg). A diagnosis of central diabetes insipidus was confirmed. The urine volume was controlled by treatment with intranasal desmopressin (10 to 15 μ g/day). Plasma PRL decreased gradually to normal ranges during 1 year from onset and there was a concomitant regression of the pituitary mass associated with partial arachnoid herniation of cerebrospinal fluid into the sella (partial empty sella) on CT and MRI^{10,11} (Figure 1c). She is currently well and is being followed in the outpatient clinic on L-thyroxine (125 μ g/day), hydrocortisone (20 mg/day) and desmopressin (10 μ g/day).

Discussion

Pituitary apoplexy is becoming increasingly recognized as a complication of pituitary adenomas, occurring in over 10% of cases.^{1,3} Manifestations typically include headache, meningeal irritation, and visual loss or ophthalmoplegia, or both, with additional features depending on the extent of spread of hypophyseal contents and haemorrhage. Multiple pituitary hormone deficiencies and/or resolution of excessive hormonal production occur in most patients with non-functioning or functioning pituitary adenomas. However, diabetes insipidus due to damage of the posterior pituitary

and/or hypothalamus, either transient or permanent, is a rare sequela of pituitary apoplexy.^{2,3}

Our patient had not only hypopituitarism and diabetes insipidus but also transient thyrotoxicosis secondary to painless thyroiditis probably as a consequence of pituitary apoplexy. One may presume that their coexistence may be fortuitous. This patient, however, had persistently positive thyroid autoantibodies, a past-history of galactorrhoea and a moderate elevation of plasma PRL thereby suggesting the pre-existing subclinical autoimmune thyroiditis and PRL producing pituitary tumour. The pathogenesis and/or trigger of spontaneous painless thyroiditis is unknown, but there is evidence of underlying changes of immune reactions related to autoimmune thyroiditis.^{4,5} Simultaneous occurrence of autoimmune Addison's disease and painless thyroiditis has been reported.¹² In this patient, primary adrenal failure was ruled out by appropriate responses to ACTH test and other endocrine functions. Maruyama *et al.*¹³ reported painless thyroiditis occurring after cessation of steroid therapy in a patient with autoimmune thyroiditis and rheumatoid arthritis. More recently, Haraguchi and colleagues¹⁴ reported painless thyroiditis occurring after unilateral adrenalectomy in two patients with Cushing's syndrome. In our patient, the pathogenic trigger for painless thyroiditis may have been immunological changes (immune rebound phenomenon)⁵ due to rapid development and/or progression of secondary adrenal failure after pituitary apoplexy.

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