Development of pituitary apoplexy during TRH/GnRH test in a patient with pituitary macroadenoma

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ABSTRACT

Pituitary apoplexy occurs as a very rare complication following pituitary function tests. Signs and symptoms are due to the rapid expansion of an infarcted and/or haemorrhagic pituitary adenoma. We report a case of macroadenoma, in which pituitary apoplexy developed 30 minutes after administration of thyrotropin-releasing hormone (TRH) and gonadotropin-releasing hormone (GnRH) injections. Magnetic resonance (MR) imaging had earlier revealed several haemorrhagic zones. After the TRH and GnRH injections, the patient complained of visual defect. MR imaging demonstrated an increase in the size of the pituitary adenoma and several haemorrhagic zones that formed a fluid-fluid level at the centre of the lesion. The pituitary mass was removed using the transsphenoidal approach. On immunostaining, follicle-stimulating and luteinising hormones were strongly positive, while prolactin was weakly positive. Pituitary functions were evaluated by dynamic function tests at six weeks post operation. The patient's pituitary functions and visual acuity were found to be normal.

Keywords: apoplexy, pituitary adenoma, pituitary function test

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INTRODUCTION

Pituitary apoplexy is a rare but life-threatening complication of pituitary adenomas.[1] Its incidence rate varies between 0.6% and 27%, and an acute or subacute form may be observed.[2-4] The symptoms include sudden and severe headaches, visual disorder, changes in consciousness level, oculomotor paralysis, visual field defects and meningismus. Despite the fact that the development of apoplexy is often spontaneous, it may also occur due to factors such as head trauma, sudden changes in blood pressure, treatment with dopamine agonists, anticoagulant treatment, antiaggregant treatment, surgery, pregnancy and thrombosis.[5] A less common reason may be pituitary stimulation tests.[6] We present a case of apoplexy that developed following a thyrotropin-releasing hormone/gonadotropin-releasing homone (TRH/GnRH) test.

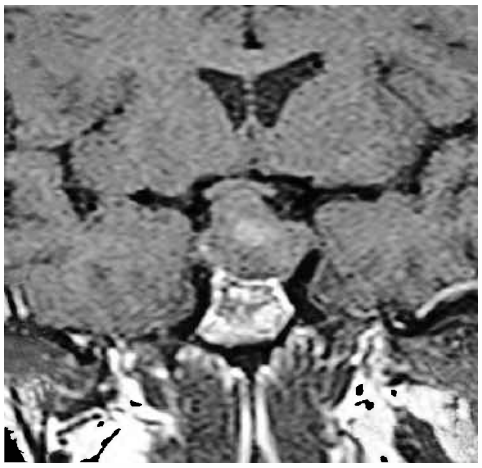

Fig. 1 Coronal T1-W MR image shows a macroadenoma compressing the optic chiasm and a haemorrhagic zone in the centre before the dynamic test.

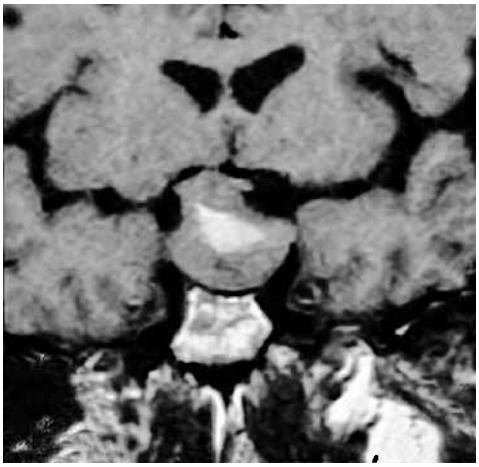

Fig. 2 Coronal T1-W MR image shows the macroadenoma with increased pituitary size and haemorrhagic zone in the centre after dynamic test. Note the increase in the tumour mass compressing the optic chiasm.

CASE REPORT

A 52-year-old male patient presented with headache

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Table I. Results of preoperative ITT, TRH and GnRH tests.

Test	Normal range	Time interval (min)				
		0	30	60	90	120
Cortisol (μg/dl)	8.00–25.00	9.88	15.33	13.88	11.61	8.30
TSH (μIU/mL)	0.35–4.94	0.99	6.41	5.86	4.76	3.87
PRL (ng/mL)	4.04–15.20	27.73	34.45	32.35	28.86	25.82
FSH (μIU/mL)	1.50–12.40	6.29	9.33	10.13	11.10	10.93
LH (μIU/mL)	1.70–8.60	3.68	13.59	13.99	13.18	10.85

ITT: insulin tolerance test; TRH: thyrotropin-releasing hormone; GnRH: gonadotropin-releasing hormone; TSH: thyroid-stimulating hormone; PRL: prolactin; FSH: follicle-stimulating hormone; LH: luteinising hormone

Table II. Results of ITT, TRH and GnRH tests at six week post operation.

Test	Normal range	Time interval (min)				
		0	30	60	90	120
Cortisol(μg/dl)	8.00–25.00	7.27	17.63	22.83	26.10	21.27
TSH(μIU/mL)	0.35–4.94	0.59	5.42	3.63	2.52	2.10
PRL(ng/mL)	4.04–15.20	11.39	30.73	20.46	15.73	15.36
FSH(μIU/mL)	1.50–12.40	6.21	9.28	10.28	10.15	10.70
LH (μIU/mL)	1.70–8.60	4.71	16.76	17.43	14.59	14.31

ITT: insulin tolerance test; TRH: thyrotropin-releasing hormone; GnRH: gonadotropin-releasing hormone; TSH: thyroid-stimulating hormone; PRL: prolactin; FSH: follicle-stimulating hormone; LH: luteinising hormone

and visual problems of six months' duration. The pituitary magnetic resonance (MR) imaging revealed a macroadenoma measuring 25 mm × 22 mm × 19 mm in size, which was compressing the optic chiasm and displacing the stalk toward the right side. T1–T2 hyperintense signal difference was seen inside the adenoma (Fig. 1). Bilateral hemianopsia was identified on visual field examination. The basal hormone levels were normal except for slight hyperprolactinaemia (Table I). An insulin tolerance test (ITT) was administered, and the results indicated adrenal insufficiency. 24 hours after the ITT test, a TRH/GnRH test was performed (Table I). Apoplexy was considered when the patient reported a temporary loss of vision 30 minutes after the injection of 200 μg TRH and 100 μg GnRH. The size of the adenoma measured 35 mm × 25 mm × 18 mm in the control pituitary MR imaging, thus presenting an increase in the lesion size from that seen in the previous MR imaging. Also, several haemorrhagic zones forming a fluid-fluid level had developed at the centre of the lesion (Fig. 2).

Emergency transsphenoidal surgery was performed within a few hours, along with steroid occluder treatment. The coagulated blood and the pituitary neoplasm were fully excised. In the postoperative period, the patient's clinical state was normal and no complications were observed. On postoperative Day 5, the patient's hormone levels were as follows: cortisol 13.14 μg/dl, prolactin 11.78 ng/mL, sT_3 1.63 pg/mL, sT_4 1.3 ng/dL, thyroid-stimulating hormone (TSH) 1.21 μIU/mL, follicle-stimulating hormone (FSH) 5.21 μIU/mL and luteinising hormone (LH) 3.59 μIU/mL. Pituitary tissue and bleeding were identified in the histopathological examination. On immunostaining, FSH and LH were strongly positive and prolactin was weakly positive. ITT and GnRH/TRH tests were repeated six weeks after the operation (Table II), and adrenal insufficiency was restored.

DISCUSSION

The TRH/GnRH test is a rare cause of apoplexy.[6] Although apoplexy can be observed in pituitary microadenoma, the majority of cases are macroadenoma.[7] The reason for apoplexy in our haemorrhagic macroadenoma patient may have been the TRH/GnRH test. The multiple risk factors for apoplexy are a decrease in the volume of blood going into the pituitary, a sudden increase in the volume of the blood going into the pituitary, stimulation of the pituitary gland, and anticoagulation.[5] Our patient suffered a macroadenoma that compressed the optic chiasm and included a haemorrhagic zone in its centre. Such haemorrhagic zones in macroadenoma are believed to develop due to ischaemic necrosis secondary to failure to meet the vascular requirement of the adenoma. Also, the growing tumour tissue may contribute to the increase in ischaemia by leading to vascular occlusion.[8] The haemorrhagic zone observed in our patient prior to the dynamic tests may have developed as a result of

this suggested physiopathogenesis.

TRH has been shown to increase the norepinephrine level. Secondary to this increase, vasospasm and pressor effect may lead to the precipitation of haemorrhages in the tumour and the development of infarcts.[9] Some researchers have claimed that TRH directly stimulates tumour cells, and the resulting increase in blood flow and volume causes a sudden growth in tumour and consequently, apoplexy.[6,9,10] Although the reasons for the occurrence of apoplexy after administration of GnRH are not clearly understood, several hypotheses exist. According to one of these, GnRH may increase the metabolic activity of the tumour and lead to the occurrence of a vascular event;[6,11] however, others claim that GnRH directly increases tumour vascularity and causes apoplexy.[12]

The temporary loss of vision observed in our patient 30 minutes after the TRH/GnRH test may have been due to the increase in the volume of the tumour, which compressed the optic chiasm in the pre-test stage. An increase in the tumour size was observed in the pituitary MR imaging following apoplexy, and the size of the haemorrhagic zone had also increased. These findings clearly indicate that the pituitary volume increases with stimulation tests and that apoplexy may develop secondary to this.

In conclusion, we believe that the presence of a haemorrhagic zone secondary to ischaemia in pituitary haemorrhagic macroadenoma patients may provide a clue for the occurrence of apoplexy, which may develop following a stimulation test. Therefore, if possible, stimulation tests should not be used in such patients. However, in special circumstances where they are absolutely necessary before an operation, the patient should be closely monitored for apoplexy, and if it does occur, an emergency pituitary decompression operation should immediately be performed under steroid treatment.

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