Spontaneous remission of acromegaly after infarctive apoplexy with a possible relation to MRI and diabetes mellitus

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Abstract

OBJECTIVES: Pituitary apoplexy is a rare clinical syndrome associated with rapid enlargement of a pituitary mass. We report the initial presentation, subsequent course and outcome of an acromegalic patient who developed spontaneous remission following pituitary apoplexy with pathologic findings of tumor infarction.
CLINICAL PRESENTATION: A 38 year-old man with typical acromegalic features was referred to our hospital. He had been diabetic and hypertensive. His basal GH and IGF-1 levels were high (80 μg/L and 747 ng/mL respectively). Sella MRI showed a macroadenoma about 19×20 mm in size. He admitted to emergency department with complains of severe frontal headache accompanied by nausea and vomiting two days after MRI was taken. His neurological examination and visual field test were normal. Emergent MRI of the sella disclosed an enhancing intrasellar mass of 24×23 mm compressing the optic chiasm. The patient underwent transsphenoidal decompression of the lesion. Histological examination revealed an adenomatous tissue showing nonhemorrhagic coagulation necrosis. Before surgery, his GH levels declined to 2.72 μg/L spontaneously and after surgery he was in remission even leading to a state of growth hormone deficiency.
CONCLUSION: When apoplexy occurs in functionning adenomas, it may cause spontaneous remission. However pituitary apoplexy due to tumor infarction is very rare. Various precipitating factors have been reported in 25–30% of pituitary apoplexy patients. Diabetes mellitus and diabetic ketoacidosis are one of these. The presence of contrast media induced endothelial swelling with the result of hypoperfusion and diabetes mellitus associated vasculopathy might be a precipitating factor in this patient.

CASE REPORT

INTRODUCTION

Pituitary apoplexy is a rare clinical syndrome associated with rapid enlargement of a pituitary mass caused by ischemic infarction or hemorrhage. It has a wide spectrum of presentations ranging from an asymptomatic state to a clinical condition with sudden onset of intense headache, ophtalmoplegia, visual field defect and altered mental state. When apoplexy occurs in functionning adenomas, it may cause spontaneous remission of adenoma. Remission of acromegaly cases have been reported before (Louwerens *et al.* 1996; Mazza *et al.* 1986; Wichers *et al.* 1997). However pituitary apoplexy due to tumor infarction is very rare. We report a case who developed spontaneous remission following pituitary apoplexy with pathologic findings of tumor infarction.

CASE REPORT

A 38 year-old man was referred to our hospital with complains of excessive sweating, joint pain, sleep apnea, decreased libido and erectile dysfunction. He also reported enlargement of his hand and foot size for about five years. He had been diabetic and hypertensive for about one year. On physical examination, the patient had typical acromegalic features. Endocrine studies revealed a high basal GH level of 80 μg/L and plasma IGF-1 level of 747 ng/mL (normal range 100–494 ng/mL). His fasting blood glucose level was found to be 393 mg/dL. Basal levels of gonodotropins were decreased but other hormone levels were within the normal range (Table 1). Sella magnetic resonance imaging (MRI) showed a macroadenoma about 19x20 mm in size enlarging the sella (Figure 1). Insulin therapy was started because of high blood glucose level.

He presented with a 2-day history of severe frontal headache, malaise accompanied by nausea and vomiting a week after insulin therapy was started and two days after sella MRI was taken. On admission to emergency department, the patient was lethargic but fully oriented. His neurological examination was normal and his visual field testing revealed no deficit. His vital signs were normal. Biochemical values revealed a blood glucose level of 330 mg/dL and a sodium level of 134 mEq/L. His urine ketone body was negative and complete blood count, liver and kidney function tests were within normal limits. Emergent MRI of the sella disclosed an enhancing intrasellar mass of 24x23 mm, extending into the suprasellar cistern and compressing the optic chiasm. (Figure 2). Patient's sodium levels began to decrease from 134 mEq/L to 127 mEq/L and glucocorticoid treatment was immediately started in suspicion of acute ACTH deficiency. Under presumptive diagnosis of pituitary apoplexy, the patient underwent transsphenoidal decompression of the pituitary lesion within 24h of admission. Histological examination revealed an adenomatous tissue composed of monotonous cells with eosinophilic cytoplasm. Most of the tissue showed nonhemorrhagic coagulation necrosis. On immunohistochemistry, most of the cells were positive for GH (Figure 3). Before surgery, his GH levels declined to 2.72 μg/L spontaneously and after surgery he was in remission even leading to a state of growth hormone deficiency (GH level <0.05 μg/L and IGF-1 level 76 ng/mL). The patient developed panhypopituitarism after surgery and he was given thyroid hormone

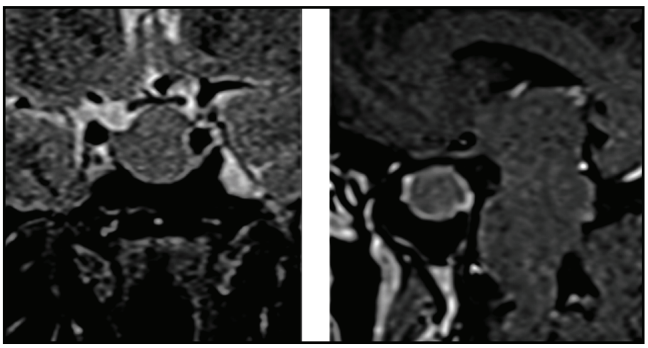

Fig. 1. The mass showing low signal intensity in T1 and T2 weighted images that's enlarging the sella.

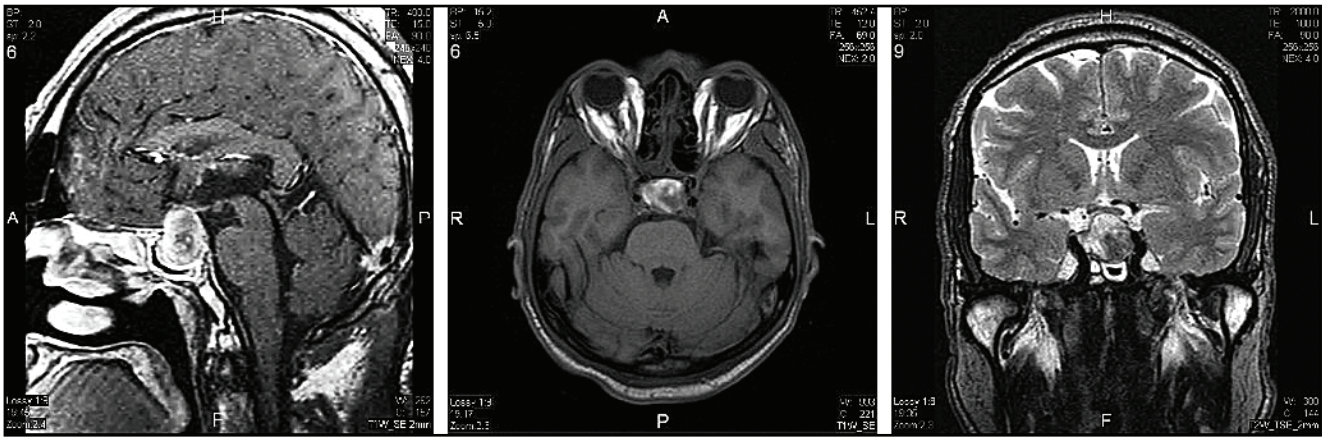

Fig. 2. The 24×23 mm-sized hyperintense intrasellar mass on T1 and T2 weighted images extending into the suprasellar cistern and compressing the optic chiasm.

and testosterone therapy. Diabetes mellitus showed improvement and the insulin dose was reduced after surgery. Sella MRI taken three months after pituitary apoplexy showed no evidence of remaining tumor.

DISCUSSION

Pituitary apoplexy usually occurs spontaneously and is often the first indication of a pituitary adenoma. The incidence of pituitary apoplexy is less than 5% with a range between 0.6% and 10% of all surgically resected adenomas. In 60–80% of cases, pituitary apoplexy occurs spontaneously without any obvious precipitating factor. Various precipitating factors leading to pituitary apoplexy have been reported in 25–30% of pituitary apoplexy patients. These include sudden trauma, use of bromocriptine, irradiation, hypertension, pregnancy, general anaesthesia, lumbar puncture, hemodialysis and several medications (anticoagulants, aspirin, chlorpromazine, isosorbide, estrogens). On the otherhand, surgical procedures including cardiac surgery, lumbar laminectomy, thyroidectomy, appendectomy have been reported to be associated with pituitary apoplexy. Neuroendocrinological manipulation and hormonal stimulation tests such as TRH and LHRH stimulation tests are other precipitating factors. Further more, diabetes mellitus and diabetic ketoacidosis have been shown to cause pituitary apoplexy. In our patient because of his high blood glucose level, insulin therapy was started only a week before pituitary apoplexy. Moreover, our patient's symptoms developed the day after sella MRI was taken. A similar case who developed pituitary apoplexy after IV injection of Gd-DTPA (dietilentriaminpentaacetic asid) for contrast enhanced MRI was reported before (Wichers *et al.* 1997). They explained this with the presence of contrast media induced endothelial swelling with the result of hypoperfusion and diabetes mellitus associated vasculopathy which might have a precipitating factor.

The slow growth of the tumor that compresses its blood supply causing ischemic infarction or hemorrhage is most likely explanation for pituitary apoplexy. Tumoral infarction is very rare. Although it was reported that the cause of pituitary apoplexy was the infarction of the gland in 22 cases of 55 patients in a study by Semple *et al.* (2006), it was reported infrequently as a cause in most of other studies. A sudden tumor growth outstripping its blood supply, radiotherapy, head injury, ischemia due to hypotension or circulatory collapse and intrinsic vasculopathy are suggested as precipitating causes which can provoke infarction. Sudden severe headache caused by the increased intracranial pressure or the retraction of dura and visual impairment caused by the rapid enlargement of the tumor growing towards the optic chiasm are the most common symptoms encountered. Clinical presentation is marked by headache in 95% of cases which may be accompanied by nausea and vomiting. On the otherhand in a retrospective study, the authors found that patients with infarctive apoplexy mechanism had less severe clinical features at presentation and a better visual outcome (Semple *et al.* 2008) Our patient also presented

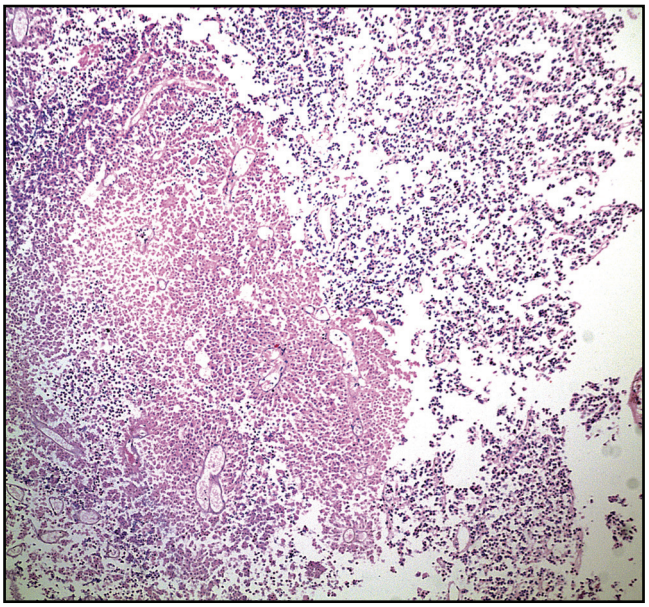

Fig. 3. The microscopic examination shows an adenomatous tissue composed of monotonous cells with eosinophilic cytoplasm. Most of the tissue shows nonhemorrhagic coagulation necrosis.

Tab. 1. Chronological changes in pituitary and target organ hormone levels.

Time	Seven days before apoplexy	The day before surgery	One month after surgery
GH (µg/L) (0.06–1)	80	2.72	<0.05
IGF–1 (ng/mL) (100–494)	747	651	76
Prolactin (ng/mL) (2.58–18.12)	19.56	1.82	1.38
ACTH (pg/mL) (0–46)	47.9		
Cortisol (µg/dL) (5–25)	16.9	5.08	
TSH (mIU/mL) (0.27–4.2)	0.616	0.854	
Free T3 (pmol/L) (3.1–6.8)	2.99	2.49	
Free T4 (pmol/L) (12.0–22.0)	16.36	16.36	
LH (mIU/mL) (1.14–8.75)	0.86	0.75	0.67
FSH (mIU/mL) (1.37–13.58)	3.44	2.48	1.07
Testosterone (ng/dL) (245–1600)	104	36.3	<20

with sudden severe headache, nausea and vomiting. However, he had no visual field defects and decrease in visual acuity in association with all these findings.

Apoplexy was found to be frequently associated with non-functioning adenomas in previous studies. However, in a recently study it was found that patients with secreting pituitary adenomas had a higher probability of developing apoplexy. They theorized that the patients with nonfunctional tumor leading to apoplexy were identified and treated only after severe symptoms developed leading to falsely elevated rate of apoplexy. Although proclatinomas are the most frequent functioning pituitary tumours, growth hormone and ACTH producing tumors predominate among the functioning pituitary tumors with apoplexy.

Patients with pituitary adenomas may recover spontaneously after pituitary apoplexy. Empty sella syndrome may also occur. A review of the literature demonstrated that pituitary deficiencies usually develop in cases after hemorrhagic apoplexy; where as normal pituitary function was retained in cases following apoplexy with non-hemorrhagic infarct. Selective infarction of adenoma leads to remission of endocrinopathy with small damage in the surrounding pituitary gland. On the otherhand, hemorrhagic apoplexy may destruct the surrounding hypophysis frequently resulting in hypopituitarism. Our patient developed partial hypopituitarism after pituitary apoplexy which showed less severe necrosis of the gland and after surgery he developed panhypopituitarism and needed hormone replacement therapy.

Indications and timing of surgery for patients with apoplexy remains controversial. It's recommended that surgical decompression should be done in patients with significant visual loss or neurologic deficits. Early decompression may partially or completely restore pituitary function.

Acute adrenal crisis due to compression or destruction of normal pituitary gland is the most life threatening endocrine disorder which is detected in two thirds of the patients with pituitary apoplexy. Thus prompt administration of corticosteroids can be life-saving maneuver. In association with this, our patient developed hyponatremia which showed improvement after administiration of glucocorticoid therapy.

There is no available data about the distinction between hemorrhagic and ischemic apoplexy. Further studies on predisposing factors of pituitary apoplexy and mechanism of tumor infarction is essential.

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