Brief Communication

Dissociated hypopituitarism after spontaneous pituitary apoplexy in acromegaly

Shahnaz Ahmad Mir, Shariq Rashid Masoodi, Mir Iftikhar Bashir, Arshad Iqbal Wani, Khalid Jamal Farooqui, Basharat Kanth[1], Abdul Rashid Bhat[1]

Departments of Endocrinology, and [1]Neurosurgery, Sheri-i-Kashmir Institute of Medical Sciences, Soura, Srinagar, Jammu and Kashmir, India

ABSTRACT

Introduction: Pituitary apoplexy is an uncommon event and usually occurs in non-functioning pituitary tumors. Among the functioning tumors, prolactinomas are the ones most likely to apoplexy. Apoplexy in growth hormone (GH) producing adenomas is a very rare event with less than thirty cases reported worldwide. **Objective:** To describe a case of spontaneous pituitary apoplexy in acromegaly. **Case Report:** A 55 year old smoker male presented to the our outpatient clinic in 2004 with complaints of gradual onset increase in the size of hands and feet, bilateral knee pain, increased sweating and blurring of vision. Investigations uncovered diabetes mellitus by a casual blood glucose of 243 mg/dl and HbA1c of 8.5%. Growth hormone suppression test using 75 gram oral glucose showed a 60 minute growth hormone of 105 ng/ml. Magnetic resonance imaging of the sellar region showed a 12.0 mm × 10.0 mm pituitary adenoma. The patient was planned for transsphenoidal tumor decompression. However, the patient was lost to follow up. Eight-years later, he presented in the emergency department of our institute with sudden onset headache, vomiting and decreased level of consciousness of one day duration. CT scan of the head with focus on the sella was suggestive of apoplexy which was later confirmed by the MRI of the sellar region. **Conclusion:** Although acromegaly can remit following apoplexy of the responsible pituitary adenoma, long term follow up is needed for early detection of the development of deficiency of pituitary hormones which may occur over years following the event as well as to detect tumor regrowth which again may occur several years later.

Key words: Acromegaly, pituitary apoplexy, pituitary macroadenoma

Introduction

Pituitary apoplexy (PA) is a neurosurgical emergency presenting with sudden onset headache, vomiting and focal neurological signs and decreased level of consciousness. Clinically apparent PA usually occurs in pituitary macroadenomas with a reported incidence being 1.6%.[1] In surgically resected adenomas, the prevalence varies between 0.6% and 10% with a mean of 2%.[2] Very often, the diagnosis of a functioning or non-functioning adenoma is made in retrospect. We describe one such case of a middle aged male who was diagnosed with acromegaly 8 years back, remained untreated, and presented with PA following, which there was resolution of growth hormone (GH) excess.

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Case Report

A 55-year-old smoker male presented to our out-patient clinic in 2004 with complaints of gradual onset increase in the size of hands and feet, bilateral knee pain, increased sweating and blurring of vision. Patient denied any history of headache. Physical examination revealed coarse facial features, large spade like hands, large feet, macroglossia, oily skin, and excessive sweating. The patient was hemo-dynamically stable with a blood pressure of 150/96 mm Hg.

Investigations revealed a normal complete blood count, liver and kidney function tests and electrolytes and evidence of left ventricular hypertrophy on electrocardiogram. Previously undiagnosed diabetes mellitus was uncovered by casual blood

Corresponding Author: Dr. Shariq Rashid Masoodi, Department of Endocrinology, Sheri-I-Kashmir Institute of Medical Sciences, Soura, Srinagar, Jammu and Kashmir, India. E-mail: shariqmasoodi@hotmail.com

glucose of 243 mg/dl and HbA1c of 8.5%. GH suppression test using 75 g oral glucose showed a 60 min GH of 105 ng/ml. The basal levels of other pituitary and target hormones are depicted in Table 1. Magnetic resonance imaging (MRI) of the sellar region showed a 12.0 mm × 10.0 mm pituitary adenoma not compressing the optic chiasm [Figure 1a]. The patient refused insulin and was started on metformin and glimepiride, and planned for transsphenoidal tumor decompression. However, the patient was lost to follow-up.

Eight years later, he presented in the emergency department of our institute with sudden onset headache, vomiting and decreased level of consciousness of 1 day duration. Examination revealed a Glasgow coma scale of 10 with right sided oculomotor nerve palsy and facial features suggestive of acromegaly. His blood pressure was 90/60 mm Hg. Subsequent investigations revealed random blood glucose of 67 mg% and normal electrolytes. Computed tomography scan of the head with focus on the sella was suggestive of apoplexy which was later confirmed by the MRI of the sellar region [Figure 1b]. The patient was initially stabilized using intravenous glucocorticoids after which a transsphenoidal tumor debulking was done. Post-surgery the patient's condition improved. His post-operative endocrine workup after the apoplexy revealed a GH (post-glucose challenge) level of 1.48 ng/ml and secondary adrenal insufficiency and central hypothyroidism [Table 1]. At present, the patient is doing well on metformin 500 mg, levothyroxine 75 μg/day and hydrocortisone 7.5 mg.

Discussion

In this report, we describe a patient in whom the diagnosis of acromegaly with diabetes mellitus was 8 years before the apoplexy. He then underwent a clinical episode strongly suggestive of acute pituitary necrosis, followed by normalization of GH levels and remission of diabetes mellitus; other pituitary functions revealed dissociated hypopituitarism in the form of central hypothyroidism, hypogonadism, and hypocortisolism.

Table 1: Hormonal analysis of the patient, before and after apoplexy

Hormone	Before PA (2004)	After PA (2012)
T4 (μg/dl)	8.9	4.2
TSH (U/L)	4.8	5.8
LH (U/L)	2.58	3.25
FSH (U/L)	4.56	2.7
PRL (ng/ml)	46.3	18
GH (ng/ml)[a]	105	1.48
Cortisol (μg/dl)	18	2.49
Testosterone (ng/dl)	282	142

PA: Pituitary apoplexy, T4: Thyroxine, TSH: Thyroid stimulating hormone, LH: Luteinizing hormone, FSH: Follicle stimulating hormone, GH: Growth hormone, PRL: Prolactin, [a]GH suppression test

PA is characterized by sudden onset headache, visual disturbance and decreased level of consciousness. Clinical remission of acromegaly following apoplexy has been reported in less than 30 cases in literature. The mechanisms proposed to explain the predisposition of pituitary adenomas to apoplexy include compression of the superior hypophyseal artery against diaphragma sellae by large pituitary tumors, friability of and increased fenestrations in the immature vessels supplying the tumor and ischemia of the adenoma because of the increasing demands on the blood supply of the growing tumor.[3] An intrinsic vasculopathy has also been incriminated in the susceptibility of pituitary adenomas to apoplexy. Lee *et al*., found markedly increased vascular endothelial growth factor in pituitary adenomas and showed positive correlation with pituitary hemorrhage.[4] Our patient had a macroadenoma at the time of diagnosis, which must have progressed over period of 8 years ultimately culminating into PA.

Apoplexy in a GH secreting adenoma leading to cure has been previously reported in literature. Tanriverdi *et al*., reported a 60 year acromegalic male who presented with panhypopituitarism and complete ophthalmoplegia without visual field defects and as in our patient, had no precipitating factors.[5] Wang *et al*., recently reviewed six patient of acromegaly in whom spontaneous remission was reported. All these cases had subclinical presentation without features of acute apoplexy and all of these patients had a nadir GH less than 1 mcg/L after 75 g oral glucose tolerance test. Therefore, cure in acromegaly is possible after PA.[3] Some patients show a remission of the underlying diabetes after PA. Our patient also had nadir GH level of 1.48 ng/ml after apoplexy and his blood glucose got easily controlled on metformin only and patient did not require any antihypertensive agent. Management of PA with mild neuro-ophthalmic signs is conservative, but requires a close and careful follow-up by endocrinologist, radiologist and neurologist. However, if neuro-ophthalmic signs fail to improve or patient shows clinical deterioration then the patient needs urgent tumor decompression by a dedicated neurosurgical unit.

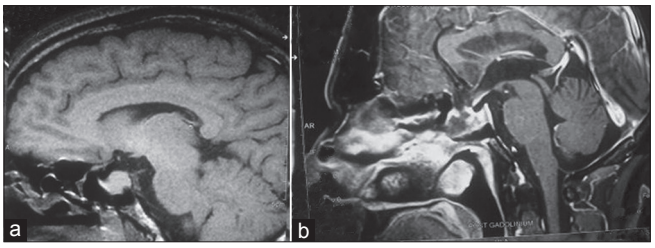

Figure 1: Magnetic resonance imaging (MRI), done 8 years before pituitary apoplexy, showing large pituitary macroadenoma 12 mm × 10.0 mm not compressing optic chiasma (a), and a recent MRI (post-gadolinium) showing features of heterogeneous pituitary hemorrhage in large adenoma (b)

Conclusion

Although acromegaly can remit following apoplexy of the responsible pituitary adenoma, long-term follow-up is needed for early detection of the development of deficiency of pituitary hormones, which may occur over years following the event as well as to detect tumor regrowth, which again may occur several years later. Significant worsening of existing headache or new onset severe headache in a patient with acromegaly should prompt a consideration of PA.

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