View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

provided by Elsevier - Publisher Connector

Kaohsiung Journal of Medical Sciences (2013) 29, 687–690

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.kjms-online.com

CASE REPORT

A case of acromegaly complicated with diabetic ketoacidosis, pituitary apoplexy, and lymphoma

He-Jiun Jiang, Wei-Wen Hung, Pi-Jung Hsiao*

Division of Endocrinology and Metabolism, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

Received 11 October 2012; accepted 8 November 2012
Available online 10 September 2013

KEYWORDS
Acromegaly;
Diabetic ketoacidosis;
Lymphoma;
Pituitary apoplexy

Abstract Acromegaly is always complicated with comorbidities and increased mortality. The disease activity and mortality outcomes are highly correlated to the level of growth hormone and insulin-like growth factor 1. A variety of clinical manifestations of acromegaly have been reported. We present a unique case where a 49-year-old male was diagnosed with acromegaly with a first manifestation as an episode of diabetic ketoacidosis. Because he refused any suggestion of treatment, a recurrent episode of diabetic ketoacidosis with pituitary apoplexy occurred. A huge B-cell lymphoma displaying as a huge facial mass followed within 1 year of the diagnosis of acromegaly. Death from advanced cancer ensued 3 years later. This clinical experience strongly reinforces the urgency of controlling growth hormone and insulin-like growth factor 1 as soon as possible once acromegaly is diagnosed.
Copyright © 2013, Kaohsiung Medical University. Published by Elsevier Taiwan LLC. All rights reserved.

Introduction

The clinical characteristics of acromegaly are mainly attributed to a sustained hypersecretion of growth hormone (GH) by pituitary adenoma. The population incidence of acromegaly is 3–4 cases per million, and its prevalence is about 60 cases per million [1,2]. Complications of acromegaly broadly involve rheumatologic arthropathies, neuropathies, cardiomyopathy, metabolic abnormalities, respiratory compromise, and neoplasia. The prognosis and outcome of acromegaly depends on whether or not it is treated [1,3].

Pituitary apoplexy is defined as pituitary hemorrhage occurring spontaneously in a preexisting nonfunctional or functional pituitary macroadenoma. Its reported incidence is very low (0.6–10.5%) [4,5]. This life-threatening consequence is a clinical challenge owing to complications

* Corresponding author. Division of Endocrinology and Metabolism, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, 100 Tzyou 1st Road, Kaohsiung 807, Taiwan.
E-mail address: pjhsiao@cc.kmu.edu.tw (P.-J. Hsiao).

1607-551X/$36 Copyright © 2013, Kaohsiung Medical University. Published by Elsevier Taiwan LLC. All rights reserved.
http://dx.doi.org/10.1016/j.kjms.2013.08.002

including severe headache, risk of vision loss, cardiovascular collapse, and endocrine crisis [6].

Overall, mortality from acromegaly has been estimated to increase 2—3-fold, and death is likely to occur 10 years earlier than in comparably healthy individuals [7]. As reported in series studies, 60% of patients died of cardiovascular diseases, 25% of respiratory diseases, and 15% succumbed to cancer [2]. The comorbidity and mortality of acromegaly are correlated to the levels of GH prior to and after treatment, the insulin-like growth factor I (IGF-1) level, and the patient's age, tumor size, degree of tumor invasion, and duration prior to diagnosis [1].

Here, we describe a patient with acromegaly first presenting with an episode of diabetic ketoacidosis (DKA). Recurrent DKA ensued concurrently with pituitary apoplexy. A malignant lymphoma grew rapidly within 1 year.

Case report

In August 2008, a 49-year-old male was sent to the emergency unit because of polyuria, polydipsia, and shortness of breath for 2 weeks. He also had a rapid body weight loss of 17 kg within 1 year. He denied any previous illness or contributory family history. DKA was diagnosed according to blood glucose of 592 mg/dL, blood ketone 4.3 mmol/L, and metabolic acidemia (pH 7.30, pCO_2 28.5 mmHg, bicarbonate14.7 mmol/L). Newly diagnosed diabetes mellitus was established by hemoglobin A_{1c} (HbA_{1c}) 17.8%, and screening for negative glutamic acid decarboxylase autoantibody.

Acromegaly was suspected because typical characteristics were noted including body height of 185 cm, body weight of 87 kg, coarse facial features, large fleshy nose, frontal bossing, jaw prognathism, acral overgrowth, and thickening skin. Acromegaly was confirmed by elevated GH 180.1 μIU/mL (normal <15 μIU/mL, equal to 5 μg/L), IGF-1 839.5 ng/mL (normal 41—272 ng/mL for males 40—50 years of age), and prolactin 293.4 ng/mL (normal 1—18 ng/mL). Imaging studies revealed sellar enlargement with a double floor contour of the sella turcica by skull X-ray and pituitary macroadenoma (1.88 cm × 1.80 cm × 2.11 cm) by magnetic resonance imaging (MRI; Fig. 1). Diabetes secondary to acromegaly was diagnosed and insulin therapy was used to control blood glucose. Transphenoidal surgical intervention was highly recommended by an experienced neurosurgeon. However, this patient refused treatment and was lost to follow-up after discharge.

Unfortunately, the patient returned to our hospital due to a sudden onset of severe headache and a recurrent DKA episode 2 months later. Pituitary apoplexy was documented by sella MRI (Fig. 2) showing a marked hemorrhage density over the pituitary macroadenoma with interval enlargement (2.20 cm × 1.96 cm × 2.00 cm). Because there was no evidence of ophthalmoplegia or pituitary failure (cortisol 9.2 μg/dL, TSH 0.76 μU/mL, Free T4 0.7 ng/dL), his condition was improved by supportive care. Surgical intervention, radiotherapy, and intensive insulin therapy were well indicated and advised during a team conference by several experts, but the patient denied further treatment again without visiting our outpatient clinic.

In June 2009, the patient visited our endocrine clinic due to a progressive bulging mass over the right face within 2 weeks. He presented with complications from hyperglycemia once again (blood glucose 764 mg/dL, blood ketone 3.4 mmol/L, and HbA_{1c} 17.5%) owing to interruption of the insulin injection. He also declared that he had sought alternative traditional herb medicine within this period. A computed tomography scan displayed a soft tissue mass 6.4 cm × 4.9 cm × 4.4 cm in size over the right maxillary sinus with extensive invasion of the sinus wall, orbital floor, nasal cavity, and cheek (Fig. 3). B-cell lymphoma was diagnosed by biopsy. His endocrine function was assessed as serum GH > 175 μIU/mL, IGF-1 823.10 ng/mL, and prolactin 196.4 ng/mL. Staging and further chemotherapy were suggested by an oncologist, but this patient still insisted on continuing his herbal medicine regimen.

In August 2012, he visited a urologist due to an enlargement of the left scrotum, intolerable dyspnea, and general weakness. Lymphoma with advanced peritoneal and pleural carcinomatosis was identified by a serial examination. The sella MRI showed interval shrinkage of the adenoma (1.46 cm × 1.80 cm × 1.80 cm). In the meantime, his GH (78.44 μIU/mL) and IGF-1 (449.18 ng/mL) declined and hypoglycemia became frequent. As a result of his intractable clinical respiratory failure, he died in September 2012.

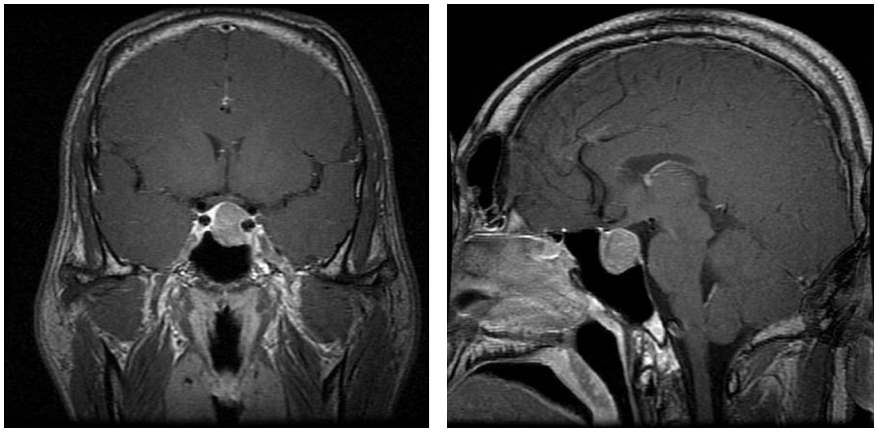

Figure 1. Pituitary macroadenoma (1.88 cm × 1.80 cm × 2.11 cm) shown in T1 phase with contrast (coronal and sagittal view) by magnetic resonance imaging.

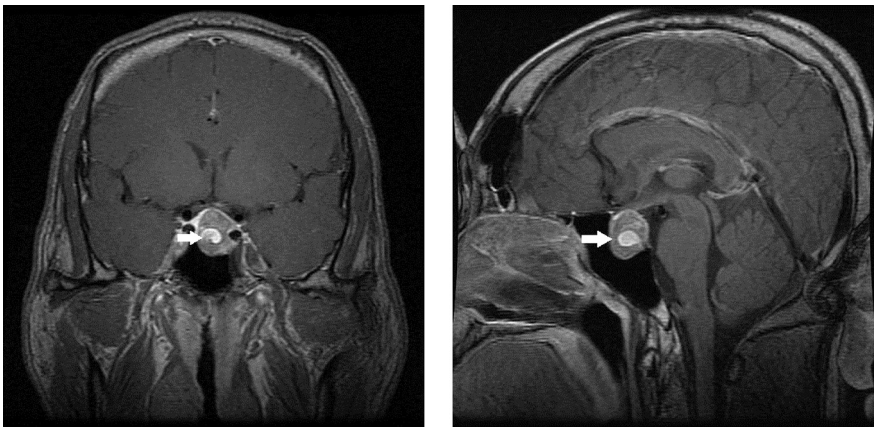

Figure 2. Pituitary apoplexy (hemorrhage marked by arrowhead) in a macroadenoma with interval enlargement (2.20 cm × 1.96 cm × 2.00 cm) shown in T1 phase with contrast (coronal and sagittal view) by magnetic resonance imaging.

Discussion

This rare case of catastrophic acromegaly proceeding rapidly to mortality provides many informative features for the clinician.

Abnormalities of glucose metabolism are common in acromegaly. Overt diabetes develops in 10—15% of patients [8]. There are many case reports of acromegaly presenting with DKA, which is attributable to insulin resistance [9]. Insulin resistance results in reduced lipoprotein lipase activity, reduced catabolism of very-low-density lipoproteins, increasing lipolysis of adipose, and increasing fatty acid influx to the liver. GH physiologically counteracts the insulin to stimulate lipolysis and promote triglyceride hydrolysis into free fatty acids [10]. Interaction between the insulin resistance and elevated GH help explain the DKA in acromegaly.

Pituitary apoplexy is a life-threatening emergency presenting as an acute episode of severe headache, visual loss, and hypopituitarism. It usually occurs spontaneously but can be predisposed by pregnancy, head injury, uncontrolled hypertension or diabetes, anticoagulant therapy, or pituitary stimulation testing [5,6]. Three mechanisms have been stated for pituitary apoplexy. First, the tumor expansion outgrows its blood supply. Second, tumor compression results in circulation extravasation beyond the dura. Third, an intrinsic aneurysm over the tumor tends to bleed [4,5]. Surgical decompression is suggested to rescue visual acuity. Hypopituitarism is supported by fluid resuscitation and hormone replacement [5]. Some cases have experienced spontaneous remission of acromegaly after pituitary apoplexy [11]. Our patient had no visual defect and hypopituitarism because of the limited hemorrhage in the adenoma, so elevated GH persisted.

Retrospective studies have reported a cancer-related mortality of 9—50% in acromegaly. Most studies have demonstrated a moderate (1.5-fold to 4-fold) increase in cancer risk in patients with acromegaly, especially neoplasms of the colon, breast, thyroid, and hematological system [7,12]. However, some investigations have not found an increased incidence of cancer mortality in acromegaly [13,14]. The inconclusive epidemiologic analyses of cancer incidence, prevalence, and mortality of acromegaly have been explained by limited case numbers and/or reporting biases. Substantial evidence has emerged to support the role of GH/IGF-1 in tumor initiation and

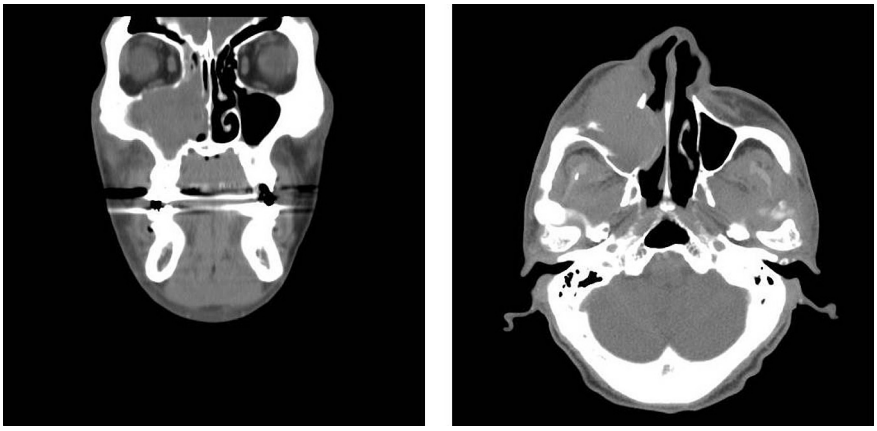

Figure 3. Computed tomography (transverse and coronal view) of the face revealed a 4.4 cm × 4.9 cm × 6.4 cm soft tissue tumor over the right maxillary sinus with invasion and destruction of the sinus wall, orbital floor, nasal cavity, ethmoid sinus, and cheek.

progression, which are synergistically mediated by the mitogenic and antiapoptotic effects of GH and IGF-1 to activate cell proliferation and transformation in many tissues. Therefore, GH/IGF-1 represents a clinical parameter to assess the disease activity of acromegaly [15]. Our patient developed a B-cell lymphoma within 1 year of his diagnosis of acromegaly and died within 3 years. The untreated status of this patient's persistent elevation of GH/IGF-1 rationally may have contributed to lymphoma formation and fatality.

Our patient presented with recurrent DKA, pituitary apoplexy, and lymphoma within 1 year after diagnosis of acromegaly. This unusual case experience of rapid progression strongly highlights the urgent necessity of controlling GH/IGF-1 as soon as the diagnosis of acromegaly is established.

References

[1] Melmed S. Medical progress: acromegaly. N Engl J Med 2006;355:2558—73.
[2] Chanson P, Salenave S, Kamenicky P, Cazabat L, Young J. Pituitary tumours: acromegaly. Best Pract Res Clin Endocrinol Metab 2009;23:555—74.
[3] Melmed S. Acromegaly pathogenesis and treatment. J Clin Invest 2009;119:3189—202.
[4] Sibal L, Ball SG, Connolly V, James RA, Kane P, Kelly WF, et al. Pituitary apoplexy: a review of clinical presentation, management and outcome in 45 cases. Pituitary 2004;7:157—63.
[5] Nawar RN, AbdelMannan D, Selman WR, Arafah BM. Pituitary tumor apoplexy: a review. J Intensive Care Med 2008;23:75—90.
[6] Turgut M, Ozsunar Y, Basak S, Guney E, Kir E, Meteoglu I. Pituitary apoplexy: an overview of 186 cases published during the last century. Acta Neurochir (Wien) 2010;152:749—61.
[7] Loeper S, Ezzat S. Acromegaly: re-thinking the cancer risk. Rev Endocr Metab Disord 2008;9:41—58.
[8] Niculescu D, Purice M, Coculescu M. Insulin-like growth factor-I correlates more closely than growth hormone with insulin resistance and glucose intolerance in patients with acromegaly. Pituitary 2013;16:168—74.
[9] Chen YL, Wei CP, Lee CC, Chang TC. Diabetic ketoacidosis in a patient with acromegaly. J Formos Med Assoc 2007;106:788—91.
[10] Vijayakumar A, Novosyadlyy R, Wu Y, Yakar S, LeRoith D. Biological effects of growth hormone on carbohydrate and lipid metabolism. Growth Horm IGF Res 2010;20:1—7.
[11] Fraser LA, Lee D, Cooper P, Van Uum S. Remission of acromegaly after pituitary apoplexy: case report and review of literature. Endocr Pract 2009;15:725—31.
[12] Jenkins PJ, Besser M. Clinical perspective: acromegaly and cancer: a problem. J Clin Endocrinol Metab 2001;86:2935—41.
[13] Orme SM, McNally RJ, Cartwright RA, Belchetz PE. Mortality and cancer incidence in acromegaly: a retrospective cohort study. United Kingdom Acromegaly Study Group. J Clin Endocrinol Metab 1998;83:2730—4.
[14] Ayuk J, Sheppard MC. Does acromegaly enhance mortality? Rev Endocr Metab Disord 2008;9:33—9.
[15] Neggers SJ, Biermasz NR, van der Lely AJ. What is active acromegaly and which parameters do we have? Clin Endocrinol (Oxf) 2012;76:609—14.