Dramatic Improvement of Diabetes Mellitus Following the Treatment of Coexisting Acromegaly and Cushing's Syndrome

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Abstract

Endocrine diseases are frequently accompanied by diabetes mellitus and treatment of an underlying endocrine disease often improves glucose control. The co-occurrence of acromegaly and Cushing's syndrome is extremely rare. We herein describe a patient who showed a dramatic improvement in glucose control following treatment for co-existing acromegaly and Cushing's syndrome. An adrenal mass was incidentally discovered during a routine evaluation of a 56-year-old woman who was subsequently diagnosed with acromegaly and a unilateral cortisol-producing adrenal adenoma. Her blood glucose was poorly controlled despite receiving high-dose insulin therapy. After undergoing adrenalectomy for Cushing's syndrome, her insulin dosage was decreased by almost 50%. The insulin treatment was discontinued following the treatment of acromegaly.

Key words: acromegaly, Cushing's syndrome, diabetes mellitus

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Introduction

Endocrine diseases, including pituitary and adrenal diseases, are frequently accompanied by the secondary occurrence of diabetes mellitus (1-3). Growth hormone (GH) and glucocorticoids can block the actions of insulin, resulting in diabetes mellitus (1, 4). There have been several studies regarding the mechanism of increased insulin resistance in acromegaly patients. Hansen et al. reported that GH may trigger insulin resistance by altering the function at the post-binding stage, and *in vitro* observations revealed that GH decreases insulin binding at high concentrations of insulin (5, 6).

Both acromegaly and Cushing's syndrome are rare diseases, making the likelihood of both occurring in one individual extremely low. To the best of our knowledge, only 5 such cases have been reported in the literature (7-11). We herein describe a 56-year-old woman with both acromegaly and a unilateral cortisol-producing adrenal adenoma who

showed a dramatic improvement in glucose control following the treatment of her acromegaly and Cushing's syndrome.

Case Report

A 56-year-old woman was admitted to the endocrinology department of our hospital for the evaluation of uncontrolled diabetes mellitus and an incidentally discovered adrenal mass. The patient had been diagnosed with diabetes mellitus five years prior. The patient denied any family history of diabetes mellitus or multiple endocrine neoplasia (MEN).

On the physical examination, the patient presented with the typical features of acromegaly and Cushing's syndrome (central obesity, moon-like face with an enlarged nose, plethora, and a sonorous deep voice). However, she had never undergone any examination specifically for acromegaly or Cushing's syndrome. After admission, the patient was diagnosed with Cushing's syndrome based on the typical clinical characteristics and laboratory findings. Her

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Figure 1. (A) Adrenal enhanced computed tomography shows a 4 cm-sized right adrenal tumor (arrow). (B) The coronal image of a gadolinium-enhanced magnetic resonance image of the pituitary gland shows a 1.5 cm-sized pituitary adenoma (arrow).

plasma adrenocorticotrophic hormone (ACTH) concentration was 4.28 pg/mL (reference range: 5-60 pg/mL), serum cortisol level was 18.28 g/dL, and her 24-hour urinary excretion of cortisol was 1,764 μ g/day (reference range: 55-286 μ g/day). In the 48-hour low-dose suppression test, the patient's plasma cortisol failed to decrease to less than 2 μ g/dL (the serum cortisol level was 15.82 μ g/dL after dexamethasone suppression). Adrenal enhanced computed tomography showed a 4 cm-sized adenoma in the right adrenal gland (Fig. 1A). The pituitary hormone tests revealed high baseline concentrations of GH (54.25 ng/mL) and insulin-like growth factor (IGF-1; 1,256.2 ng/mL). The other hormone results showed an elevated prolactin level (82.13 ng/mL), a decreased level of thyroid stimulating hormone (TSH; 0.04 mIU/L), a normal level of free thyroxine on the lower end of the range (0.94 ng/dL) and decreased levels of luteinizing hormone (LH; 0.10 mIU/mL), follicle stimulating hormone (FSH; 0.43 mIU/mL), and estradiol (5.0 pg/mL). A 75 g glucose load did not reduce the GH concentration to $\leq$ 1 μ g/L. Brain magnetic resonance imaging (MRI) showed a 1.5 cm-sized pituitary tumor (Fig. 1B).

Thyroid sonography showed a thyroid nodule, which was shown to be benign following fine-needle aspiration cytology. At admission, the patient was receiving multiple-dose insulin injection therapy using the basal-bolus regimen (120 units of insulin glargine + 32 units of insulin glulisine three times a day + 1,000 mg metformin) for glucose control. However, her fasting blood glucose concentration was never lower than 200 mg/dL.

The right adrenal tumor was resected in February 2008. Four weeks later, her blood glucose concentration improved, and we reduced her total insulin dosage from 216 to 130 units a day. After adrenalectomy, the hormone results indicated an elevated prolactin (129.7 ng/mL), a normal level of TSH on the lower end of the range (0.80 mIU/L) with a normal level of free thyroxine (1.15 ng/dL), and decreased levels of LH (0.10 mIU/mL) and FSH (0.89 mIU/mL) with

a low level of estradiol (5.0 pg/mL). The ACTH level was 29.42 pg/mL, and the cortisol level was 6.71 μ g/dL, 15.46 μ g/dL, and 16.42 μ g/dL at 0, 30, and 60 min, respectively, after the ACTH stimulation following right adrenalectomy. The patient was placed on steroid replacement therapy (prednisolone, 2.5-5 mg per day) for 5 months after adrenalectomy. The steroid replacement therapy was stopped after normalization of the cortisol response.

The surgical removal of the pituitary macroadenoma was delayed by the patient for personal reasons. Five years later, at 63 years of age, the patient underwent selective transsphenoidal removal of the pituitary adenoma. After removal of the pituitary macroadenoma, the hormone tests revealed a low prolactin level (1.68 ng/mL), a normal level of TSH in the lower end of the range (0.42 mIU/L), a normal level of free thyroxine (1.52 ng/dL), and low levels of LH (2.29 IU/mL), FSH (12.29 mIU/mL), and estradiol (7.4 pg/mL). Over the next month, her total insulin dose was markedly reduced from 74 to 30 units per day (30 units of insulin glargine + 1,000 mg metformin). The insulin therapy was subsequently discontinued due to repeated episodes of hypoglycemia, and the patient took only metformin (1,000 mg/day) (Fig. 2). A 75 g glucose load suppressed her GH concentration to $<$ 1 μ g/L, thus indicating that her acromegaly had been cured.

Discussion

In the present study, the patient had two interesting characteristics. The first was the co-occurrence of acromegaly and Cushing's syndrome. This unusual presentation may be due to an endocrine syndrome, such as MEN or Carney's complex, as demonstrated in previous studies. Alzahrani et al. (11) described Cushing's syndrome as the initial manifestation of MEN type 1 (MEN 1). Their case, contrary to ours, showed the evidence of hyperparathyroidism (12). Our patient had normocalcemia, normal parathyroid and pancreas

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