中文題目：對口服葡萄糖具反應性之腎上腺庫欣氏症：病例報告

英文題目：OGTT responsive adrenal Cushing's syndrome presenting with unsuppressed ACTH: A case report

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Introduction

Adrenal Cushing's syndrome typically presents with high serum cortisol levels and suppressed adrenocorticotropic hormone [ACTH] levels. Studies have revealed that abnormal or ectopic expression of adrenal receptors for various hormones, may regulate cortisol production. Herein, we present a case of Cushing's syndrome whose serum cortisol concentration is responsive to oral glucose stimulation, suggesting the presence of aberrant hormone receptor, such as gastric inhibitory polypeptide [GIP] receptor; and whose ACTH remains unsuppressed, which is less common for Cushing's syndrome caused by a unilateral adrenal adenoma.

Case report

The 71-year-old woman with hypertension and hyperlipidemia was diagnosed as type 2 diabetes mellitus since one year ago. She accidentally found a left adrenal mass when receiving the abdominal sonography due to abdominal fullness for a month. The patient also presented with body weight gain, dorsal fat pad, and thin skin recently. Laboratory data showed elevated 24-hour free urine cortisol (704.5 ug/day) and loss of diurnal change of serum cortisol (8 am & 10pm: 10.2 & 14.5 ug/dL) as well as ACTH (8 am & 10 pm: 15.0 &15.2 pg/mL). Low dose dexamethasone suppression test showed unsuppressed serum cortisol level (4.0 ug/dL), confirming the diagnosis of Cushing's syndrome.

To determine the etiology of Cushing's syndrome with unsuppressed ACTH levels, serial examinations were performed to differentiate Cushing's disease and ectopic Cushing's syndrome, including desmopressin [DDAVP] test, corticotropin releasing hormone [CRH] test and high dose dexamethasone suppression test. The test results showed unsuppressed serum and urine cortisol levels under high dose dexamethasone, unstimulated ACTH and cortisol levels after DDAVP injection, discordant results for ACTH and cortisol levels after CRH injection, suggesting the possibility of ectopic Cushing's syndrome. There was also no obvious space-occupying lesion in bilateral pituitary glands on magnetic resonance imaging [MRI] sella imaging. Therefore, bilateral inferior petrosal sinus sampling [BIPSS] was performed and the ratio of petrosal/peripheral ACTH levels was < 2, indicating a non-pituitary source of cortisol secretion.

In order to find an ectopic source for cortisol secretion, chest computed tomography [CT], abdominal MRI, and whole body positron emission tomography [PET] imaging were completed. A 1.2 cm right upper lung tumor was disclosed on chest CT and whole body PET. Surgical pathology revealed adenocarcinoma, with negative ACTH stain. Post-operative morning cortisol level was 4.2 ug/dL, indicating non-remission of Cushing's syndrome. Reviewing the patient's profile and abdominal CT of a left 1.9 cm adrenal mass, ACTH-independent adrenal Cushing's syndrome was

also considered. Therefore, norcholesterol [NP-59] adrenal scan was arranged and a left side functional adrenal adenoma was found.

For survey of aberrant expression of hormone receptors in adrenal Cushing's syndrome, thyrotropin-releasing hormone [TRH] test, luteinising-hormone releasing hormone [LHRH] test and oral glucose tolerance test [OGTT] were performed. The results of TRH and LHRH tests were unremarkable, but serum cortisol level rose significantly from 5.0 to 22.5 ug/dL 30 minutes after oral 75g glucose loading. Octreotide can have modest effect in controlling cortisol hypersecretion in such cases but the patient preferred surgery. Left adrenalectomy was performed smoothly in May, 2019 and the pathology report revealed a benign adenoma without positive ACTH staining. Post-operative serum cortisol level was < 0.4 ug/dL, indicating remission of Cushing’s syndrome. The patient is currently under cortisone replacement therapy and her symptoms related to Cushing’s syndrome has gradually improved.

Clinical lesion

Cushing’s syndrome caused by an adrenal adenoma is typically associated with suppressed ACTH levels < 5 pg/mL. However, it should be kept in mind that ACTH levels between 10-20 pg/mL can be present in the two forms, both ACTH dependent and independent Cushing’s syndrome. Evaluation of aberrant hormone receptors can be performed in cortisol-producing adrenal adenomas and bilateral macronodular adrenal hyperplasia. Ectopic expression of gastric inhibitory polypeptide receptor [GIP-R] may result in OGTT responsive or food responsive Cushing’s syndrome.