Abstract
Context. We report the use of subcutaneous somatostatin injection three times a day to decrease hypercortisolism in a patient who had Cushing’s syndrome induced by bronchial carcinoid tumour progressive pneumonia due to immune suppression.

Subject and Method. A 46-year-old man with 7-month history of DM type-2, hypertension and cerebrovascular-disease, vertebral compression-fracture was admitted to our clinic. Physical examination was consistent with Cushing’s syndrome. Laboratory results revealed hyperglycemia (143 mg/dL; reference range, <100 mg/dL) and hypokalemia (2.29 mEq/L; reference range, 3.5-5.1 mEq/L). His morning serum cortisol was 40 µg/dL (reference range 6.7-22.6 µg/dL), urine cortisol-excretion was 2245 µg/24 hours (reference range 58-403 µg/24 hours), after 1 mg dexamethasone-suppression test serum cortisol was 28 µg/dL (reference range 6.7-22.6 µg/dL) and ACTH 354 pg/mL (reference range 7.9-66 pg/mL). Adrenal CT and hypophyseal MRI were normal. An ectopic source was searched for Cushing’s syndrome. Chest CT scan of the right lung showed 12x9 mm nodule. High fever cough occurred on the follow-up. Chest radiograph revealed diffuse pneumonic infiltration. Despite 3-drug antibiotic combination therapy, infection did not improve. Subcutaneous injection of octreotide 3x100 µ/g was initiated to decrease hypercortisolism. The infection improved rapidly after the therapy. The morning serum cortisol, urine cortisol-excretion, ACTH was at the upper normal range (77.1 pg/mL, reference range 7.9-66 pg/mL) on 10th day of treatment. The patient was a consulted for surgery and the nodule was excised. The pathology was consistent carcinoid tumor.

Conclusion. Subcutaneous octreotide treatment may be helpful to gain time for exploring the focus in ectopic cushing’s syndrome and to control the serious infections due to hypercortisolism.

Key words: Ectopic Cushing’s syndrome, octreotide, carcinoid tumor.

INTRODUCTION

Cushing’s syndrome can be clinically presented as glucose intolerance, hypertension, osteoporosis, proximal muscle weakness, thromboembolic
When iatrogenic causes are excluded, the most common cause of Cushing syndrome is Cushing disease (pituitary-dependent) accounting for approximately 70% of cases, adrenal adenomas are responsible for about 10-15% of cases and carcinomas for less than 5%. In 15% of cases, Cushing syndrome may be associated with non-pituitary tumors secreting ACTH the ectopic ACTH syndrome. On clinical grounds, this can be divided into two entities, cases occurring in the setting of highly malignant tumors such as small cell carcinoma of bronchus and mere indolent cases occurring in patients with underlying neuroendocrine tumors such as bronchial carcinoids (1). We report the use of subcutaneous somatostatin injection three times a day to decrease hypercortisolism in a patient who had Cushing’s syndrome induced by a bronchial carcinoid tumour.

**CASE**

A 46-year-old man with 7-months history of diabetes mellitus type 2, hypertension and cerebrovascular disease was presented to our hospital because of lumbago, leg weakness and difficulty in walking for 4-months. He was operated 1-month ago on vertebral compression fracture diagnosed in thoracolumbar MRI. He was admitted to our endocrinology clinic because of redness and swelling of the face and diabetes mellitus. On physical examination he had moon facies, facial plethora, bilateral pretibial edema and diffuse ecchymoses on the arms and abdomen (Fig. 1). His vital signs showed a blood pressure of 160/90 mmHg, rhythm was regular and heart rate was 102 per minute. Muscle strength was 1/5 at right lower extremity and 2/5 at the left. Laboratory results revealed hyperglycemia (143 mg/dL; reference range, <100 mg/dL) and hypokalemia (2.29 mEq/L; reference range, 3.5-5.1 mEq/L). His morning serum cortisol was 40 µg/dL (reference range 6.7-22.6 µg/dL), ACTH 354 pg/mL (reference range 7.9-66 pg/mL), urine cortisol excretion was 2245 µg/24 hour (reference range 58-403 µg/24 hour), after 1 mg dexamethasone suppression test serum cortisol was 28 µg/dL (6.7-22.6). The other biochemical parameters were normal. Surrnal CT and hypophyseal MRI were reported normal. An ectopic source was searched for Cushing’s syndrome. Chest CT scan of the right lung showed a 12x9 mm nodule in the middle lobe. PET-CT scan performed. Increased metabolic activity was detected on the left side of prostate gland in PET-CT scan and malignancy was excluded by biopsy. While laboratory tests were going on, high fever, cough and phlegm occurred on the follow-up.

*Figure 1. Moon facies and ecchymoses on the skin before treatment (Left), Healthy image after treatment (Right).*
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Posteroanterior chest radiograph revealed diffuse pneumonic infiltration on the left and right lung. Diffuse consolidation in the right lung (Fig. 2), lower lobe and inferior lingula segment of the left lung and bilateral pleural effusion were seen in chest CT scan (Fig. 2). Despite 3-drug antibiotic combination therapy, infection did not improve. Subcutaneous injection of octreotide (3x100 µg) was initiated to decrease hypercortisolism. The infection improved rapidly after the therapy. There was an acute response on laboratory parameters. Ten days after, the pulmonary infection improved, morning serum cortisol was normalized, urine cortisol-excretion decreased, and the ACTH was at the upper normal range. Therapy was stopped and 1 week later octreotide scintigraphy was performed. There was a focal octreotide uptake on the middle and lower zone of the right lung (Fig. 3). The patient was consulted for surgery and the nodule was excised. The pathology was consistent with carcinoid tumor (Fig. 4). Adrenal insufficiency developed in postoperative period and prednisolone initiated. The insulin therapy was stopped and antihypertensive drugs were gradually tapered. Muscle strength ameliorated and the patient began to walk (Fig. 1).

**DISCUSSION**

The morbidity and mortality depends on excess cortisol release in Cushing’s syndrome. Hypercortisolism can lead to several medical problems like hypertension, obesity, osteoporosis, fractures, poor skin healing, infectious diseases, glucose intolerance and
Figure 4. Pathological image of carcinoid tumors. A - ovoid and round cells with dense core granules in the cytoplasm; B - spherical nodule with a well-defined and slightly lobulated border.
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psychosis (2-3).

ACTH can be produced outside the pituitary in a benign or malignant tumor in the lung, thymus gland, pancreas, or other organ. This is called “ectopic” ACTH production or ectopic Cushing’s syndrome. Besides ACTH, these tumours were shown to secrete a number of biologically active hormones and precursors, that could cause Cushing’s syndrome. Corticotrophin releasing hormone, corticotrophin-like intermediate lobe peptide, ACTH precursors, and pro-opiomelanocortin were among the described factors (4). Ectopic Cushing’s syndrome is more common because of the high rate of lung cancer, but it often goes unrecognized. Ectopic Cushing’s syndrome due to malignancy may ameliorate when the underlying pathology is solved (1).

Medical therapy may be necessary to reduce the cortisol levels, depending on prognosis of malignancy and the treatment plans. Medical therapy may be reasonable if the tumor cannot be excised or prognosis is poor. Ketoconazole, metyrapone, mitotane and somatostatin are the medical agents that can be used for the treatment of hypercortisolism.

Rapid treatment may be necessary in ectopic Cushing’s syndrome. There was not enough time for operation of lung nodules in our patient. He was in a poor state because of infection. Resistant infections due to hypercortisolism require early intervention. Somatostatin receptors can be detected by scintigraphy in 80% of ectopic ACTH-releasing tumors. For this reason somatostatin analogue octreotide may be useful in ectopic Cushing’s syndrome treatment by reducing ACTH production. There was a dramatic amelioration 5 days after the initiation of octreotide 3x100 mcg/day. Uwaifo et al. reported clinic and laboratory improvement after somatostatin therapy in 3 patients with ectopic Cushing’s syndrome and resistant to steroidogenesis inhibitors (5). Bruno et al. reported a reduction of corticotropin levels and adrenal insufficiency with octreotide treatment for 3 years to attenuate recurrent hypercortisolism in a 40-year-old female patient with an ectopic ACTH-producing carcinoid tumor (6). Van den Bruel et al. reported metabolic control for 8 years with octreotide treatment in a patient with ACTH-releasing lung carcinoid tumor (7).

In conclusion, subcutaneous octreotide treatment may be helpful to gain time for exploring the focus in ectopic Cushing’s syndrome and to control the serious infections due to hypercortisolism.

Conflict of interest
We declare that there is no conflict of interest.

References
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