The case of Cushing’s disease imaging by SPECT examination without manifestation of adenoma in MRI examination

Marcin Gierach, Joanna Pufal, Stanisław Pilecki, Roman Junik
Laboratory of Nuclear Medicine of the Department of Endocrinology and Diabetology of the Ludwik Rydygier Collegium Medicum, Bydgoszcz, Poland

[Received 30 V 05, Accepted 11 X 05]

Abstract:
BACKGROUND: The aim of our study was to evaluate the possibility of imaging the pathological accumulation of 99mTc-MIBI in the pituitary gland in patients with Cushing’s disease when MRI examination does not show microadenomas.
MATERIAL AND METHODS: Cushing’s disease was diagnosed in a 27 year old male on the basis of clinical and biochemical findings. The blood cortisol level of the patient was elevated (the average level was 47 ug/dl) and it showed no changeability of day and night rhythm.
RESULTS: In the patient with Cushing’s disease, during the SPECT examination, an increased accumulation of 99mTc-MIBI in the pituitary gland was noticed. MRI scanning was negative.
CONCLUSION: Single photon emission computed tomography using 99mTc-MIBI is a useful and sensitive means of pituitary gland microadenoma detection in patients with Cushing’s disease when microadenoma is not detected during MRI scanning and when the results of dexamethasone suppression test is positive.
Key words: Cushing disease, SPECT, MRI

Introduction
Cushing’s syndrome, which also includes Cushing’s disease, is caused by overproduction of cortisol, which results in the following symptoms: central obesity along with weight gain to the neck and upper back (buffalo hump) and hanging dewlap, muscle weakness, thin skin, flushed face, purple stretch marks, pain in the sacrum area connected with osteoporosis and compression fractures of vertebrae, arterial hypertension (especially in over 40-year-olds), impaired glucose tolerance or diabetes mellitus, mental changes — depression, maniacal excitement, psychosis and suicidal susceptibility, and in women — hyperandrogenism with irregular menstrual periods and hirsutism [1]. Untreated hypercortisonism causes shortening of the lifespan (average 7–10 years). Thus, the most important thing is to reduce the blood cortisol concentration to the correct values. This can be done by the use of “biochemical knife ” — medicines such as: mitotane, amnoglutethimide and ketoconazole, which cause suppression of cortisol production at the level of 21-L-hydroxylase, this leads to the removal of symptoms caused by hypercortisonism (the symptoms of vascular hemorrhagic diathesis, ecchymosis and thrombus, bacterial and mycotic infections, arterial hypertension, diabetes mellitus and mental changes). However, these medicines are hepatotoxic and cause other complications such as: hypotension, hyponatremia, hypokaliemic alkalosis, hypofunction of suprarenal and thyroid glands. Thus, these drugs are only used during the period of preparation for surgery (removal of the pituitary microadenomas, ectopic tumour etc.).

The dexamethasone suppression test confirms the location of the excessive cortisol secretion. In the case of incomplete suppression of cortisol secretion a pituitary location can be suspected, then MRI examination with gadolinium enhancement of the pituitary gland should be performed. However, adenomas are visualized only in 50–70% of cases with MRI scanning [2–6]. In 30–50% of cases, the confirmation of the dexamethasone suppression test by MRI examination is negative (it does not show any
pathological changes in the pituitary gland) despite the clinical features of the disease.

Many case reports about accumulation of Tc99m-MIBI in tumours and adenomas, as well as in pituitary glands, have been performed [7], but, to our best knowledge, the case of accumulation of Tc99m-MIBI in the pituitary gland of patients with Cushing’s disease, confirmed by the dexamethasone suppression test, has not yet been described in literature.

The aim of our study was to show the possibility of imaging the pathological accumulation of 99mTc-MIBI in the pituitary gland in patients with Cushing’s disease when MRI examination does not show microadenomas, and when the dexamethasone suppression test confirms the location of microadenomas in the pituitary gland.

Material and methods

Cushing’s disease in a 27-year-old male had been diagnosed on the basis of clinical and hormonal findings. The blood cortisol level of the patient was elevated (the average level was 47 µg/dl) and it showed no changeability of day and night rhythm. The suppression test with dexamethasone showed a decrease from 20.5 µg/24 hours to 12.2 µg/24 hours.

No abnormalities in the pituitary gland were observed during MRI scanning in the patient. The patient underwent pituitary SPECT using 99mTc-MIBI. The control group consisted of 5 volunteers without hormonal dysfunction of the pituitary gland, who underwent 99mTc-MIBI SPECT because of coronary heart disease.

The patient and control groups were examined on a single-head-gamma-camera Diacam (Siemens, Erlangen, Germany) with a low-energy high-resolution collimator (LEHR, low energy high resolution) was used while measuring the emission from the pituitary glands by computed tomography. The acquisition was started 2 hours after intravenous administration of 600 MBq of 99mTc-MIBI. The head was rotated round each subject’s head by 360 degrees on an elliptical course divided into 64 projections of 30 seconds each, matrix size 128 × 128. Attenuation correction was not performed. Reconstruction was performed utilizing a Butterworth filter, cut-off 0.4, slices reconstructed every two pixels. The analysis of SPECT images was both qualitative and semi-quantitative. The regions of interest in each pituitary gland were drawn and then the radiotracer uptake was compared with the uptake in the region of interest of parietal bone, which was accepted as 100% uptake by 360 degrees on an elliptical course divided into 99mTc-MIBI. The head was rotated round each subject’s head was started 2 hours after intravenous administration of 600 MBq of 99mTc-MIBI. The acquisition was started 2 hours after intravenous administration of 600 MBq of 99mTc-MIBI. The head was rotated round each subject’s head by 360 degrees on an elliptical course divided into 64 projections of 30 seconds each, matrix size 128 × 128. Attenuation correction was not performed. Reconstruction was performed utilizing a Butterworth filter, cut-off 0.4, slices reconstructed every two pixels. The analysis of SPECT images was both qualitative and semi-quantitative. The regions of interest in each pituitary gland were drawn and then the radiotracer uptake was compared with the uptake in the region of interest of parietal bone, which was accepted as 100% uptake.

Results

In the patient with Cushing’s disease, during the SPECT examination, an increased accumulation of 99mTc-MIBI in the pituitary gland was noticed (Figure 1). After the SPECT examination, the patient underwent operation, which confirmed our findings.

In the pituitary glands of patients of the control group, accumulation of the radiotracer was not observed. No accumulation was noticed in other parts of the brain, except for the choroidal plexus, in any of the examined control group. Accepting the radiotracer uptake in parietal bone to be 100%, we noted that accumulation in the pituitary glands of the patient with Cushing’s disease was 148%.

Discussion

Single photon emission computed tomography (SPECT) is one of the tomography techniques that image the morphology and function of organs by displaying them in thin sections [8, 9, 10]. The physical basis of the method is a registration of gamma radiation quanta emitted by radioisotopes of medium length half-life: usually technetium-99m, sometimes thallium-201, indium-111, iodine-123 and occasionally xenon-133 and krypton-77.

In normal conditions, technetium 99mTc-MIBI does not cross the blood–brain barrier. However, the radiotracer has the ability to penetrate damaged barriers [11]. The uptake of the radiotracer depends on both the number of mitochondria and the potentials of mitochondrial and cellular membranes [12]. Therefore, cells with high metabolic activity such as neoplastic tissues can show high levels of the radiotracer uptake [7]. The pituitary gland SPECT examination connects a local examination with an estimation of gland activity in some tumours.

The sensitivity of scintigraphy techniques is high, but the specificity of this method is rather low. The uptake of 99mTc-MIBI was observed in some intracranial tumours such as astrocytoma, glioblastoma and meningioma [11]. Some of the adenomas also show increased metabolic activity, which was used in scintigraphic investigations — for example the parathyroid glands. Because of the difficulties in adenoma location during MRI, we decided to confirm the existence of an adenoma in the pituitary gland of the patient with Cushing’s disease during the 99m-Tc-MIBI SPECT examination.

We observed that no 99mTc-MIBI uptake is demonstrable in intracranial normal structures (except choroid plexus), as noted in previous studies [11]. No abnormalities in the pituitary gland had been observed during MRI scanning in the examined patient with Cushing’s disease. The SPECT examination showed the presence of an adenoma.
Conclusion

Single photon emission computed tomography using 99mTc-MIBI is a useful and sensitive means of pituitary gland microadenoma detection in patients with Cushing's disease when microadenoma is not detected during MRI scanning, and when the results of dexamethasone suppression test is positive.

Therefore, SPECT examination should be admitted as a complementary diagnostic method when microadenoma of the pituitary gland is suspected.

References