CASE REPORT

Adrenocortical Carcinoma Treated by CyberKnife

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Abstract

Adrenocortical carcinoma is a rare malignancy with a poor prognosis. The effective treatment for advanced cancer remains unknown. A 61-year-old woman underwent CyberKnife treatment on a large adrenocortical carcinoma and tumor emboli in both pulmonary arteries. Follow-up positron emission tomography scanning with fluorodeoxyglucose (FDG) revealed that the FDG uptake was greatly decreased in all the tumors, and the hormone levels were also decreased. CyberKnife is a safe and effective treatment option for the non-operative large advanced adrenocortical carcinoma.

Key words: adrenocortical carcinoma, CyberKnife, radiation therapy

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Introduction

Adrenocortical carcinoma is a rare malignancy with an incidence of 0.7-2.0 cases/million inhabitants/year (1). The prognosis is very poor. The tumor-node-metastasis (TNM) classification proposed by the European Network for the Study of Adrenal Tumors classification is recommended (2), in which stage IV is defined by the presence of distant metastasis, with an estimated five-year disease-specific survival rate of 13%. Complete surgical resection is the only potentially curative treatment for adrenocortical carcinoma (3), and there is no curative treatment for unresectable cancer.

To the best of our knowledge, this is the first report of the successful CyberKnife treatment for primary adrenal cancer in Japan.

Case Report

A 61-year-old woman presented with syncope when she bent forward to pick up a heavy package. She had a medical history of hypertension. She had noticed virilization within a few months. Abdominal CT revealed a large mass measuring 98×79×100 mm, consistent with a large adrenal tumor, and mass emboli in the bilateral pulmonary artery and small mass lesions in the lungs (Fig. 1, 2). The adrenal tumor infiltrated to the left adrenal vein, the left renal vein and then into the inferior vena cava. Positron emission tomography (PET) scanning with fluorodeoxyglucose (FDG) revealed an increased FDG uptake in this tumor and also in the mass emboli and the mass lesions in the lungs, which was consistent with large adrenal cancer with pulmonary embolism and pulmonary metastasis (Fig. 3). The adrenocorticotropic hormone (ACTH) level was undetectable and the cortisol level was 29.1 μg/L. A low-dose dexamethasone suppression test revealed hypercortisolism according to the undetectable ACTH level and an un-suppressed cortisol level of 24.1 μg/L. Because the patient did not exhibit any characteristic features of Cushing’s syndrome, such as a fatty hump between the shoulders, rounded face or red stretch marks on the skin, she was diagnosed with subclinical Cushing’s syndrome. The serum aldosterone level was elevated to 299.2 pg/mL, however, the potassium level was 4.7 mEq/L and the plasma renin activity was 18.9 ng/mL/h, thus aldosterone-producing adenoma was ruled out. The dehydroepiandrosterone sulfate (DHEA-S) level was markedly increased to 2,170 μg/L, which was suggestive of adrenocortical carcinoma along with the findings of PET scanning.

The emboli in the bilateral pulmonary artery appeared to be a mixture of thrombus and tumor, as they exhibited calcification, and the D-dimer level was elevated to 4.9 μg/L. A vascular echogram of the lower limbs revealed a thrombus measuring 3 mm in the right soleal vein, therefore we speculated that the cause of the pulmonary embolism was

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According to the above findings, the patient was diagnosed with stage IV adrenocortical carcinoma due to multiple lung metastases. The pulmonary embolism and infiltration to the inferior vena cava put her at a high risk of complications by general anesthesia. The patient refused chemotherapy and opted for CyberKnife treatment of the adrenal cancer and pulmonary emboli.

The patient underwent CyberKnife treatment for the adrenal cancer and paraaortic lymph node swelling. The tumor volume was 483 cm$^3$ and the prescribed radiation dosage was 45 Gy, 15 fractions with 61% isodose line. She subsequently underwent another CyberKnife treatment for the pulmonary emboli. For the embolus of the right pulmonary artery, the tumor volume was 27 cm$^3$ and the prescribed radiation dosage was 35 Gy, 7 fractions with 76% isodose line. For the embolus of the left pulmonary artery, the tumor volume was 24 cm$^3$ and the prescribed radiation dosage was 36 Gy, 6 fractions with 72% isodose line. During the treatment for the pulmonary emboli, anticoagulation therapy with heparin and warfarin was started. After two weeks, the thrombus in the right soleal vein disappeared, the D-dimer level decreased to within the normal range, and warfarin was continued thereafter.

Four months later the patient had no symptoms and her general condition was excellent. Her blood pressure was...
normal without medication, and virilization was not observed. The cortisol level normalized to 17.9 μg/L and DHEA-S decreased to 1,542 μg/L, which was 70% of the pre-treatment level. FDG-PET showed that the FDG uptake was remarkably decreased in the tumor, the emboli, and the paraaortic lymph node (Fig. 4).

**Discussion**

There is no effective treatment for stage IV adrenocortical
cancer. Mitotane is currently the only potential treatment. However, our case showed that CyberKnife is a promising and safe treatment option for this devastating cancer.

In 1990, Luton et al. studied 105 patients with adrenocortical carcinoma and reported the clinical features and the effect of mitotane therapy (4). They concluded that the first therapeutic approach to adrenocortical carcinoma is surgical resection even in patients with extensive metastatic disease, and radiotherapy is ineffective and should be considered only as palliative treatment for metastatic disease, whereas mitotane should be used as adjuvant therapy after aggressive surgery despite the lack of a significant effect on the survival. However, a recent review of various studies showed that the objective response rate of mitotane treatment is at best 24% (5). A large-scale international study, the first international randomized trial in locally advanced and metastatic adrenocortical carcinoma treatment (FIRM-ACT) trial, showed that patients who received mitotane plus a combination of etoposide, doxorubicin, and cisplatin had a higher response rate than those in the streptozocin-mitotane group (23.2% vs. 9.2%), although there was no significant difference in the overall survival (6). Another disadvantage of mitotane is that it has a narrow therapeutic window and adverse effects occur in more than 80% of all patients and are often dose-limiting (7). Even the most promising chemotherapy has unsatisfactory effects on this cancer, and patients suffer from serious adverse effects.

In the pertinent literature, there are only two reports on CyberKnife treatment for adrenal tumor: a retrospective analysis of 26 patients from China (8), and that of 4 patients from India (9). The former study included 8 cases of primary adrenal tumors and 18 cases of metastatic adrenal tumors, with 3 patients achieving CR, 12 patients with PR, 5 patients with stable disease, and 6 patients with progressive illness in 3 months. The average tumor volume was 72.1 cm\(^3\) and the prescribed radiation dosage ranged from 30-50 Gy (8). The latter report from India was the treatment on adrenal metastasis, with 2 patients achieving CR and 2 patients with PR in 2-3 months. The median gross tumor volume (GTV) was 20.5 cm\(^3\) and the minimum dose of GTV ranged from 12.1-31.1 Gy (9). None of the cases had a giant tumor, as in our case, yet they showed favorable results with minimal complications. There are some other reports of CyberKnife treatment on adrenal metastasis, however, radiotherapy is still not recommended for primary adrenal cancer.

This is the first case report of CyberKnife treatment on a giant adrenocortical carcinoma for which other treatment was ineffective or not recommended.

The adrenal gland is adjacent to the kidney, stomach, pancreas, and intestines. The delivery of large radiation doses with high spatial precision is crucial to avoid the radiation injury to the surrounding healthy tissues. CyberKnife is one type of stereotactic radiosurgery systems which deliver beams of high-dose radiation to tumors with extreme accuracy. Our case underwent CyberKnife treatment for a large unresectable tumor and pulmonary emboli and achieved PR with no complications. All the symptoms resolved and the patient was able to return to her normal life at 6 months after the therapy. CyberKnife is a very effective and safe treatment to control adrenocortical carcinoma and can improve the patients’ quality of life.

The authors state that they have no Conflict of Interest (COI).

References