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Metastatic Pituitary Tumor From Renal Cell Carcinoma Treated by Fractionated Stereotactic Radiotherapy—Case Report—

Takakazu YOKOYAMA, Atsuo YOSHINO, Yoichi KATAYAMA, Takao WATANABE, Yoji KASHIMA*, Tetsuo YOSHIKAWA**, Jiro KAWAMORI***, and Yoshiaki TANAKA***

Departments of Neurological Surgery, *Ophthalmology, **Urology, and ***Radiology, Nihon University School of Medicine, Tokyo

Abstract

A 63-year-old man presented with rapidly progressive visual field deficit and hypopituitarism including diabetes insipidus, 8 years after treatment for a renal cell carcinoma. Neuroimaging studies revealed a dumbbell-shaped pituitary mass that had destroyed the sellar floor and abutted against the optic apparatus. Fractionated stereotactic radiotherapy (SRT), employing computer-image integration techniques and a frame that could be relocated to facilitate a fractionated dosing scheme, was carried out under a plan for reducing the treatment risk to the optic apparatus. Three months later, the patient exhibited marked improvement in the visual field deficit and visual acuity concomitant with a reduction in tumor volume. Magnetic resonance imaging of the sellar region confirmed striking shrinkage of the metastasis. His neurological status remained stable at 12 months after the SRT with no complications. Fractionated SRT appears to be effective for preserving or improving the residual vision in patients with visual loss secondary to metastatic tumor of the pituitary gland, and may result in a longer and better quality of life.

Key words: pituitary, pituitary metastasis, fractionated stereotactic radiotherapy, metastatic tumor, renal cell carcinoma

Introduction

Metastatic tumor of the pituitary gland occurs in 1% to 4% of all cancer patients in large autopsy studies.13,18–20 Moreover, most pituitary metastases are asymptomatic.18,29 Only 6.8% of pituitary metastases in an autopsy series were symptomatic.30 A review of 220 cases, including cases from the literature, found that the origin was the breast in 49.8%, the lung in 20.2%, the gastrointestinal tract in 6.4%, the prostate gland in 6.0%, melanoma in 2.3%, and others accounted for less than 2.0%.19 Symptomatic pituitary metastasis from renal cell carcinoma (RCC) is very rare and only a few cases have been reported in large pituitary metastasis series to date.24,26 RCC is the most common primary tumor of the kidney and accounts for 1% to 3% of adult malignancies.6,26

The brain is the fourth most common site for metastasis after the lung, bone, and liver. However, only 4% to 13% of patients develop brain metastases during the course of RCC.17,23

We describe a case of symptomatic pituitary metastasis secondary to RCC treated by image-guided fractionated stereotactic radiotherapy (SRT).

Case Report

A 63-year-old male presented at our neurological surgery department with a history of progressive visual field deficit and headache persisting for a few months on December 27, 2001. His past history included treatment for a RCC (6 cm in diameter, clear cell subtype) of the right kidney by right radical nephrectomy (pT2b, grade I) on December 14, 1993. Subsequently, he did not have to attend the urology department and did not receive any radiation therapy, chemotherapy, or hormonal treatment until 5 years later. He had no complaints of symptoms and his clinical status remained stable. However,
Fig. 1 Visual fields revealing bitemporal hemianopsia (upper row), and dramatic improvement of the visual field defect after treatment (lower row).

Fig. 2 Sagittal (left) and coronal (right) magnetic resonance images with gadolinium showing a homogeneously enhanced dumbbell-shaped pituitary mass with suprasellar extension and a small indentation at the level of the diaphragma sellae, which compresses the optic apparatus.

chest roentgenography indicated multiple pulmonary metastases on December 16, 1998. He underwent systemic administration of α-interferon (600 × 10⁴ IU/day × 2 times/wk) after the multiple pulmonary metastases had been confirmed by bronchoscopy and cytology. However, this agent was not used continuously because anorexia and depression were frequently observed. Nevertheless, his clinical status remained stable until he presented at our department.

Ophthalmological evaluations revealed bitemporal hemianopsia and diminished visual acuity (Fig. 1 upper row). His best corrected visual acuity was 10/20 in the right eye and 14/20 in the left eye. No other cranial neuropathy and urological symptoms were present except for excess thirst and polyuria (urine volume, more than 5 l/day; specific gravity, less than 1.005). Plasma electrolyte analysis indicated electrolytic disturbance caused by diabetes insipidus (sodium level, 152 mEq/l). His plasma hormone levels were as follows: prolactin, 3.9 ng/ml (normal range, 1.5–9.7 ng/ml); growth hormone, 0.24 ng/ml (<0.42 ng/ml); insulin-like growth factor-1, 23 ng/ml (42–250 ng/ml); adrenocorticotropic hormone, 14 pg/ml (7.4–55.7 pg/ml); cortisol, 1.5 µg/dl (4.0–18.3 µg/dl); thyroid-stimulating hormone, 2.15 µIU/ml (0.50–5.00 µIU/ml); free T3, 0.99 pg/ml (2.30–4.30 pg/ml); free T4, 0.31 ng/dl (0.90–1.70 ng/dl); luteinizing hormone, 0.2 mIU/ml (1.8–5.2 mIU/ml); and follicle-stimulating hormone, 1.5 mIU/ml (2.0–8.2 mIU/ml). These data were almost consistent with panhypopituitarism. Consequently, replacement hormone therapy was initiated with levothyroxine, hydrocortisone, and desmopresin.

Skull radiography showed destructive erosion of the floor and dorsum sella turcica. Computed tomography (CT) of the head disclosed an intrasellar and suprasellar mass that had destroyed the bony floor and posterior wall of the sella turcica. Magnetic resonance (MR) imaging revealed a dumbbell-shaped mass filling the sella, extending into the suprasellar cistern with an indentation at the level of the diaphragma sellae and abutting against the optic apparatus, but not entering the cavernous sinus (Fig. 2). No other metastatic sites were evident within the brain. Cerebral angiography demonstrated massive tumor staining, fed by the bilateral internal carotid arteries.

Our patient showed the signs of early appearance of diabetes insipidus and visual field deficit with a history of cancer, and MR imaging revealed a dumbbell-shaped pituitary mass with a clear indentation at the level of the diaphragm. Therefore, the diagnosis was metastasis to the pituitary gland from RCC, based on these quite indicative clinical and radiological findings.1,8,28,29)

The treatment procedures for fractionated SRT were based on computer-image integration techniques with a frame that could be relocated to facilitate the fractionated dosing scheme, as described previously.32) In brief, a Gill-Thomas-Cosman relocatable frame (Radionics, Burlington, Mass., U.S.A.) was used for securing the head,71)
Three-dimensional treatment planning view enabling easy avoidance of critical structures such as the brain stem, optic nerves, and optic chiasm. Semitransparent green shows the 65% isodose volume. The fractionated stereotactic radiotherapy dose plan used two isocenters and three arcs for each isocenter. The treatment consisted of 8 daily fractions of 3.5 Gy to the 65% isodose line and a total dose of 43.1 Gy with minimized dose delivery to the optic apparatus.

The treatment plan was designed using the XKNIFE-4 treatment-planning software program (Radionics). Since the tumor was close to critical normal tissue such as the optic chiasm, optic nerves, brain stem, and cavernous sinus, the Linac gantry rotation orbit and the rotational angles were planned to reduce the doses to these critical regions. Employing two isocentric movements of the Linac gantry, the 4 MV Linac radiation beam (MEVATRON M2-6745; Toshiba, Tokyo) was converged onto the tumor volume (5.44 cm³). The collimator size for the isocenters was 2.5 cm and 1.25 cm, and three rotational arcs were used for each isocenter. The treatment consisted of 8 daily fractions of 3.5 Gy to the 65% isodose line and a total dose of 43.1 Gy. As a result, the optic chiasm was exposed to a mean total dose of 208.8 cGy (range, 88.6–401.3 cGy), the left optic nerve to 108.5 cGy (5.1–432.1 cGy), and the right optic nerve to 90.7 cGy (5.0–368.2 cGy). The treatment risk to the optic apparatus was thereby reduced to a minimum (Fig. 3).

The prescribed radiation dose treatment was completed without the occurrence of any acute morbidity on January 31, 2002. The patient remained in stable condition for several months except for transient deterioration of visual acuity observed at one month after SRT (1.4/20 in the right eye and 2/20 in the left eye). Three months later, his visual field deficit and visual acuity exhibited marked improvement. Ophthalmological evaluations confirmed restoration of vision in both eyes (10/20 in the right eye and 14/20 in the left eye). MR imaging demonstrated shrinkage of the pituitary tumor on May 23, 2002. The mass effect of the pituitary metastasis on the optic apparatus was diminished, explaining the improvement in visual symptoms. He slipped and fell in the road and broke his right humerus on July 1, 2002. A pathologic fracture was later identified. Subsequently, he was readmitted to our hospital on July 30, 2002, with severe pains in both femurs caused by widespread bone metastases, which were treated by radiotherapy.

The most recent follow-up examination on December 28, 2002, 12 months after the initial diagnosis of a metastatic tumor of the pituitary gland, showed the diabetes insipidus and hypopituitarism persisted, but he remained clinically stable. The bitemporal hemianopsia and diminished visual acuity (14/20 in the right eye and 24/20 in the left eye) were significantly improved concomitant with dramatic shrinkage of the pituitary tumor (Figs. 1 lower row and 4).

Discussion

Metastatic tumor of the pituitary gland tends to be diffuse, invasive, and hypervascular, and is difficult to resect safely and curatively even with the use of modern microneurosurgical techniques. The proximity of skull base lesions to critical structures, such as the optic nerve and the cranial nerves of the cavernous sinus, requires special care to accomplish delivery of the optimum curative radiotherapy dose to the lesion while avoiding excessive exposure of these structures. These features and the rarity of symptomatic metastatic tumor of the pituitary gland may be the reason that little has recently been reported regarding the optimal treatment.

Stereotactic radiosurgery has recently gained popularity compared to surgical resection, since this method can be applied to any site in the brain for high efficiency, non-invasive treatment, with a
Fig. 4 Sagittal (upper row) and coronal (lower row) magnetic resonance images with gadolinium at 2 (left column), 4 (center column), and 10 months (right column) after fractionated stereotactic radiotherapy. Marked shrinkage of the tumor was clearly evident at 4 months. The tumor remained dramatically reduced in size at 10 months. Diminished mass effect of the pituitary metastasis resulted in the improvement in visual field deficit and visual acuity.

short hospitalization time, small number of adverse effects, and cost-effectiveness.4,27) The term “stereotactic radiosurgery” was coined by Leksell in 1951 to describe a method of destroying diseased or dysfunctional tissue with a single large dose of radiation delivered stereotactically by focused narrow beams,15) but the method only entered clinical use in 1971, with the design of the gamma knife system.26) The principle was transferred to modern linear accelerators in the 1980s.4,9) Linear accelerator-based stereotactic radiosurgery was multiple arc radiotherapy to deliver an even high dose to the target and rapid dose fall-off in normal tissues.9)

Fractionated SRT, using a linear accelerator, may allow the administration of radiation with high accuracy dose per fraction and afford a further radiobiological advantage by fractionating the prescribed dose.22) Such radiotherapy may thus be well suited to pituitary metastases. On the other hand, the effect of fractionated SRT on metastatic lesions from RCC is unclear, since primary RCC has traditionally been considered as a “radiation-resistant” tumor.19,21) A smaller tumor reduction rate (27%)20) and a lower complete response rate (11%)21) were found in patients with RCC brain metastases. Conversely, stereotactic radiosurgery showed similar or better effectiveness (local control rate, 81.5–100%) on RCC brain metastasis than on other histologies.2,3,5,10,23)

Direct treatment of pituitary metastases should focus on symptomatic relief and prevention of neurological deterioration.24) Conventional radiotherapy for pituitary lesions exposes the optic apparatus and adjacent normal tissues to large radiation doses which may cause radiation necrosis and damage. In contrast, stereotactic irradiation can minimize the dose to the optic apparatus and adjacent normal tissue because of the sharply focused dose distribution. In addition, fractionated SRT has a further radiobiological advantage in that damage to the normal tissue will be reduced.32) The optic nerve, the most delicate nerve structure for radiotherapy, can tolerate a dose per fraction of 1.8 Gy to a total dose...
of 45 to 54 Gy or a single dose of 6.5 to 10 Gy.14,25,31 Parameters such as the dose per fraction and overall treatment times are very important in both the curative efficacy and occurrence of adverse side effects,25,31 but the details remain largely unexplored and unreported to date.

In the present case, the treatment consisted of 8 daily fractions of 3.5 Gy to the 65% isodose line and a total dose of 43.1 Gy using two isocenters, whereas the mean dose volumes delivered to the optic chiasm, left optic nerve, and right optic nerve were minimized to 208.8 cGy, 108.5 cGy, and 90.7 cGy, respectively. As a result, the patient demonstrated improvement in his visual fields and acuity concomitant with a reduction of tumor volume within 3 months of completion of the treatment. Furthermore, no tumor progression and no other severe treatment-related complications were noted. However, the risk of delayed optic neuropathy remains of concern.14,31 As is known from conventional fractionated radiotherapy, the latency period between the radiation therapy and the first signs of injury to the visual pathway is 6 to 50 months, with 90% of patients developing radiation-related optic neuropathy within the first 3 years after radiation therapy.7,14 The follow-up period in the present case is still too short to assess the long-term risk of radiation-related optic neuropathy. Furthermore, a longer follow-up period is needed to confirm the durability of the tumor control and visual preservation.

Although it is difficult to draw any firm conclusions from a single case, fractionated SRT appears to be effective for preserving or improving the residual vision in patients with visual loss secondary to metastatic tumor of the pituitary gland, and may result in a longer and better quality of life. Further studies are needed to evaluate the use of fractionated radiotherapeutic regimens for tumors that are not suitable for radiosurgery or surgical resection in patients requiring intervention.

References

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Address reprint requests to: A. Yoshino, M.D., Department of Neurological Surgery, Nihon University School of Medicine, 30–1 Oyaguchi–kamimachi, Itabashi–ku, Tokyo 173–8610, Japan.
E-mail: ayoshino@med.nihon-u.ac.jp

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