LARGE CENTRAL LESIONS COMPRESSING THE HYPOTHALAMUS AND BRAINSTEM : OPERATIVE APPROACHES AND COMBINATION TREATMENT WITH RADIOSURGERY

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Abstract : A major aim of minimally invasive neurosurgery is to preserve function in the brain and cranial nerves. Based on previous results of radiosurgery for central lesions (19 craniopharyngiomas, 46 pituitary adenomas, 9 meningeal tumors), combined micro- and/or radiosurgery was applied for large lesions compressing the hypothalamus and/or brainstem. A basal interhemispheric approach via superomedial orbitotomy or a transcallosal-transforaminal approach was used for these large tumors. Tumors left behind in the hypothalamus or cavernous sinus were treated with radiosurgery using a gamma unit. Preoperative hypothalamo-pituitary functions were preserved in most of these patients. Radiosurgical results were evaluated in patients followed for more than 2 years after treatment. All 9 craniopharyngiomas decreased in size after radiosurgery, although a second treatment was required in 4 patients. All 20 pituitary adenomas were stable or decreased in size and 5 of 7 functioning adenomas showed normalized values of hormones in the serum. All 3 meningeal tumors were stable or decreased in size after treatment. No cavernous sinus symptoms developed after radiosurgery. We conclude that combined micro- and radio-neurosurgery is an effective and less invasive treatment for large central lesions compressing the hypothalamus and brainstem.

Key words : Pituitary adenoma, Craniopharyngioma, Hypothalamus, Operative approach, Radiosurgery

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INTRODUCTION

A major aim of minimally invasive neurosurgery is the preservation of functions of the brain and cranial nerves. Radiosurgery is a powerful and less invasive treatment for deep-seated lesions, especially in eloquent areas of the brain such as the sensorimotor cortex, thalamus, basal ganglia and cavernous sinus^{1~4}). However, large tumors or tumors compressing the optic pathway, hypothalamus and brainstem are not suitable for radiosurgery⁵). Recent microsurgical and skull base techniques have facilitated radical resection of tumors in and around the hypothalamus and brain-

stem by several approaches such as orbitozygomatic, cavernous, petrosal, condyl and supra- or infrafacial triangle approaches^{6~11}). However, complications and morbidity remain problematic in patients with these tumors.

We have applied a combination of micro- and radiosurgery to the treatment of central lesions compressing the hypothalamus and/or brainstem as a minimally invasive treatment to preserve preoperative brain functions. Our operative approaches and the results of this combination treatment are described in this report.

Fig. 1 Basal interhemispheric infrachiasmatic approach via superomedial orbitotomy shown on the MR image of a patient with a huge craniopharyngioma.

Fig. 2 Transcallosal-transforaminal approach shown on the MR image of a patient with a huge pituitary adenoma.

CLINICAL MATERIAL AND METHODS

Patient Population

Between May 1991 and December 1997, 74 patients with central lesions in the brain and skull base were treated with radiosurgery using a gamma unit. Lesions included 19 craniopharyngiomas, 46 pituitary adenomas and 9 meningeal tumors. A removal operation was performed in most patients and residual or recurrent tumors were treated with radiosurgery. Combination treatment was indicated in patients with large central lesions compressing the hypothalamus and/or brainstem or in patients with pituitary adenoma invading into the cavernous sinus. Removal operation using several approaches depending on the site, size and shape of the tumor was planned for patients with large lesions. Radiosurgery was indicated for residual tumors in and around the hypo-

thalamus and pituitary stalk. Transsphenoidal removal was planned in most patients with pituitary adenoma and any residual tumor in the cavernous sinus was to be treated with radiosurgery. Parasellar lesions such as cavernous sinus or clinoid meningioma were excluded from this study.

Operative Approach

Transsphenoidal, pterional and orbitozygomatic approaches were used for intrasellar, suprasellar and/or parasellar tumors as usual.

A basal interhemispheric approach via superomedial orbitotomy (Fig. 1) was used for large tumors compressing the hypothalamus upwards and/or occupying the third ventricle and/or compressing the midbrain backwards. Since the optic chiasm was usually displaced superiorly, there was a wide area in the prechiasmatic space. The undersurface of the

Fig. 3 MR images of a patient with craniopharyngioma (same as Fig.1). a : Preoperative MR image showing a large tumor compressing the optic pathway and hypothalamus. b : Postoperative MR image showing normal appearance of the hypothalamus and a small residual tumor at the suprasellar region. Visual and hypothalamo-pituitary functions were preserved. The residual tumor was treated with radiosurgery.

Fig. 4 MR images of a patient with craniopharyngioma. a : The large tumor occupying the third ventricle and extending into the interpeduncular cistern. b : Postoperative MR images showing a small intra- and suprasellar residual tumor.

chiasm, hypothalamus and pituitary stalk were easily detected during the tumor removal procedure though the infrachiasmal route. This approach was also taken via the suprachiasmal route (trans-lamina terminalis) when tumors occupied the third ventricle or when the chiasm was of prefixed type.

A transcallosal-transforaminal approach was used for large tumors occupying the third ventricle and extending downwards to the interpeduncular and pre-pontine cisterns (Fig. 2). Since the lateral ventricle and foramen of Monro were dilated in patients with these tumors, there was a wide corridor to the cistern. It was possible to widen the foramen by partial resection of the unilateral fornix anteriorly or dissection of the septal vein to the venous angle posteriorly when the

foramen was not sufficiently wide. After removal of the tumor in the third ventricle, the cistern was opened at the floor of the ventricle. The third nerve, posterior communicating artery, P1 segment of posterior cerebral artery, basilar artery and superior cerebellar artery were recognized in the cistern. When the tumor extended downwards to the level of the lower pons, the vertebral union and bilateral vertebral arteries were also exposed.

Radiosurgery

The optic pathway is most sensitive tissue to radiosurgery. Less than 10 (recently less than 8) Gy was planned to be delivered to the pathway. Marginal isodose for tumors was intended to be more than 50%.

A marginal dose was planned to be more than 10Gy for craniopharyngiomas, more than 12Gy for meningiomas and more than 18Gy for pituitary adenoma, particularly in functioning adenomas. Thin-sectioned axial and coronal MR images were examined during radiosurgery to obtain figures of the optic pathway. A thin-sectioned CT scan was also examined for detection of the optic canal.

RESULTS

Microsurgery for Large Tumors

Twenty patients with large central lesions received 36 operations for tumor removal because of residual or recurrent tumors. These tumors included 8 pituitary adenomas, 7 craniopharyngiomas, 3 meningiomas and 2 malignant tumors. Six of 8 patients with pituitary adenoma received transsphenoidal operation as the first treatment and 2 had a second transsphenoidal operation. However, large residual or recurrent tumors in the suprasellar region necessitated a second or third operation in these 6 patients. A basal interhemispheric

approach was used finally in all 8 patients with pituitary adenoma and one also received treatment by a transcallosal-transforaminal approach. Three of 7 patients with craniopharyngioma received a second or third operation because of recurrence. A basal interhemispheric approach was used in 6 patients and a transcallosal-transforaminal approach was used in 2 patients. The other 5 patients with meningioma or other histology received a basal interhemispheric approach and 2 required a simultaneous pterional approach.

Nineteen patients who underwent a basal interhemispheric approach showed headache, visual disturbance, endocrinopathy (amenorrhea, polyuria, obesity, emaciation, etc.) and amnesia preoperatively. Total or subtotal tumor removal was performed in most patients (Fig. 3) and preoperative functions were improved or unchanged in all patients except for enlargement of a visual field defect in one patient with a calcified craniopharyngioma and hypopituitarism which required replacement therapy (cortisol and thy-

Fig. 5 MR images of a patient with recurrent GH-producing adenoma. a: The tumor was treated with gamma knife radiosurgery. b: Gd-enhanced MR image 5 years after radiosurgery showing shrinkage of the tumor. The GH value in the serum was normalized 3 years after treatment.

Fig. 6 MR images of a patient with residual craniopharyngioma. a: Preradiosurgical MR image showing a cystic tumor in the third ventricle. b: The tumor decreased in size 6 months after gamma knife radiosurgery and was stable 3 years after treatment.

roid hormone). Nine patients required no replacement therapy postoperatively.

Three patients treated by a transcallosal-tranforaminal approach showed headache, visual disturbance, endocrinopathy and disturbance of consciousness preoperatively. Subtotal or 80% partial removal (residual in suprasellar region) was obtained (Fig. 4) and no hypothalamic damage was recognized. All three patients had hypopituitarism preoperatively and required replacement therapy postoperatively.

To date 11 of 20 patients have received gamma knife radiosurgery after microsurgery as the indicated combination treatment for residual tumors in functional areas. These were 6 craniopharyngiomas, 3 pituitary adenomas and 2 meningeal tumors. A marginal dose of more than 10, 12 and 18Gy for craniopharyngioma, meningioma and pituitary adenoma, respectively, was obtained in all patients except one mesenchymal tumor in the hypothalamus. This tumor adhered to the hypothalamus close to the optic chiasm. The residual tumor was treated with marginal dose of 9 Gy.

Radiosurgery

Thirty-two of 74 patients treated were followed for more than 2 years after radiosurgery. Twenty of these 32 patients had pituitary adenoma which was treated with a marginal dose of 9 to 35Gy (mean 19Gy). Seven patients received less than 18Gy (9 to 16Gy) as a marginal dose because of the size and close association with the optic pathway. Six tumors were non-functioning and one GH-producing adenoma received 16Gy. Three of 7 tumors decreased in size and one showed decreased hormonal activity after treatment. Although the other 4 tumors showed no changes for 3 to 5 years, 3 were removed by a transsphenoidal approach thereafter. Thirteen tumors were treated with a marginal dose of 18Gy or more. These included 7 non-functioning, 5 GH-producing and 1 ACTH-producing adenoma. Eight tumors decreased in size and 5 remained stable (Fig. 5). Five of 6 patients with a functioning adenoma showed normalization of hormonal activity including a marked decrease in body weight in a patient with Cushing's disease.

Nine patients with craniopharyngioma were treated with a marginal dose of 9 to 15Gy (mean 10.6Gy), 2 of whom required a second treatment. Two patients received less than 10Gy (9Gy) as a marginal dose because the tumors were in contact with the optic chiasm. In 5 patients including 2 patients with a marginal dose of 9Gy, tumors decreased in size (Fig. 6). One patient who was 9 years old at the time of radiosurgery developed menstruation 2 years after

treatment. Four patients required a second or third treatment, although all tumors decreased in size. In 2, recurrence appeared from the cystic part of tumor which was excluded from the first treatment. Regrowth of tumor appeared outside of the treated area in one patient. All 4 retreated patients are well and have the same quality of life as before treatment.

Two patients with meningioma were treated with a marginal dose of 15 and 16Gy, respectively. Both tumors were stable 2 years after treatment. One patient with mesenchymal tumor in the hypothalamus was treated with a marginal dose of 9Gy. The tumor decreased in size 2 years after treatment.

A transient adverse effect of radiosurgery developed in one patient with craniopharyngioma 6 months after treatment. His visual acuity decreased for 2 months and recovered thereafter. No other cranial nerve dysfunction including superior orbital fissure or cavernous sinus symptoms have been recognized to date.

DISCUSSION

Between May 1991 and December 1997, we have treated 750 patients with radiosurgery using a gamma unit. Although a longer follow-up study is required, we have found that radiosurgery is a quite safe and effective treatment for many lesions. However, remaining problems of radiosurgical treatment include a difficulty in the treatment of relatively large lesions, latency before obliteration, and undue effects such as brain edema, cyst formation and radiation injury¹²⁻¹⁴. Although new technical developments such as staged treatment or aminosteroid therapy¹⁵ may help address these problems, we are now treating AVMs, acoustic tumors, craniopharyngiomas, meningiomas, pituitary adenomas, metastatic brain tumors and functional disorders by a gamma unit alone or in combination with microsurgery or intravascular surgery. For radiosurgical treatment of central lesions, we must consider the histology of lesions and dose limitation since the optic pathway may be close to the lesions. The marginal dose delivered is important for optimal treatment of each lesion. Although the number of patients treated in this study was small, the results of follow-up studies for more than 2 years suggest that a marginal dose of more than 10, 12 and 18Gy seems to be necessary for the treatment of craniopharyngioma, meningioma and pituitary adenoma, respectively. These data are essential for the combination treatment of large central lesions compressing the optic pathway, hypothalamus and brainstem.

Recent microsurgical techniques and skull base approaches have effectively decreased the mortality rate for surgical treatment of large central lesions. To

obtain a better view in and around the basal and interpeduncular cistern to reduce morbidity, we developed a basal interhemispheric approach via superomedial orbitotomy¹⁶⁾. Furthermore, a transcallosal-transforaminal approach¹⁷⁾ was introduced for large lesions occupying the third ventricle and extending downwards to the interpeduncular and prepontine cisterns. The basal interhemispheric infrachiasmatic approach effectively exposes the undersurface of the optic chiasm, tract and hypothalamus. The pituitary stalk is exposed from the exit of hypothalamus to the entrance of sella turcica. The inner surface of the hypothalamus is also exposed by the suprachiasmatic approach. A view in and around the interpeduncular cistern is obtained by basal interhemispheric or transcallosal-transforaminal approaches. The later approach also enables exposure of the prepontine cistern. Although aggressive surgery for tumor removal is possible using these approaches, we have employed a combination treatment for the preservation of hypothalamo-pituitary functions. Histologic re-evaluation of peritumoral tissues of craniopharyngiomas has revealed normal neural tissue without a glial barrier. Therefore complete removal of the craniopharyngioma without neural damage is not possible in such cases, especially in large tumors¹⁸⁾. In this series, the part of the tumor in the hypothalamus was left in 7 of 20 patients (4 large craniopharyngiomas, 2 huge pituitary adenomas, 1 mesenchymal tumor). Preservation of preoperative hypothalamo-pituitary function was obtained in all patients except one. Residual tumors were treated with radiosurgery in 5 of 7 patients. Two patients with residual pituitary adenoma have been followed clinically and under MR imaging studies without treatment.

The recurrence rate after subtotal removal of central lesions (craniopharyngioma, pituitary adenoma and meningioma) remains problematic over a long follow-up period. Radiosurgery provides a potential alternative treatment for these residual tumors. Long-term follow-up results for radiosurgical treatment of these central lesions are required. In this series, the results of a follow-up of more than 2 years have been evaluated. In pituitary adenomas treated with a marginal dose of 18Gy or more, the result was satisfactory as shown in MR imaging studies of tumor volume and endocrinologic examinations for functioning adenomas. No adverse effects were recognized during the follow-up period. In the patient with the longest follow-up of 5 years and 10 months, a GH-producing adenoma decreased in size and the GH value normalized after radiosurgery. No signs of recurrence have been evident based on MR images and endocrinologic

examinations to date. However, undue effects on pituitary functions, internal carotid artery and cranial nerves in the cavernous sinus should be carefully evaluated over a longer period^{19,20)}.

The radiosurgical results of craniopharyngioma were encouraging because all tumors responded, at least within the treated portion. No recurrence appeared in 5 patients up to 5 years. However, 4 tumors recurred from outside the treated areas including the cystic part which is treatable with radioactive materials²¹⁾. Although all patients including re-treated patients retained equivalent activities to before treatment, long-term follow-up studies are required in these patients. Detection of the non-enhanced part of tumors on MR image during radiosurgery is difficult but is important for prevention of recurrence, as well as for prediction of recurrence from residual tumors after gross total resection of the tumor.

This series was too small for the evaluation of the radiosurgical results of meningioma. However, we have treated 100 patients with meningioma since 1991. Sixteen patients were followed for more than 5 years (data not shown). These tumors were treated with a marginal dose of 9 to 25Gy (mean 14.3Gy). Seven of 16 tumors decreased in size and 9 were unchanged after radiosurgery. Perifocal brain edema developed in one patient but later recovered. No tumors recurred except for 3 atypical meningiomas. Although longer follow-up studies are required, our results suggest that radiosurgery is effective for meningiomas, in line with previous reports^{22,23)}.

CONCLUSION

Although further studies are required, the results of radiosurgery for central lesions show promise regarding the treatment of residual tumors after subtotal resection of large tumors. Basal interhemispheric and/or transcallosal-transforaminal approaches are useful for removal of these large tumors and for functional preservation. We conclude that combined micro- and radiosurgery is an effective and less invasive treatment for large central lesions compressing the hypothalamus and brainstem.

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