Hypophysial transposition (hypophysopexy) for radiosurgical treatment of pituitary tumors involving the cavernous sinus

Technical note

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Stereotactic radiosurgery (SRS) is performed with increasing frequency in the treatment of residual or recurrent pituitary adenomas. Its major associated risk in these cases of residual or recurrent pituitary tumor adjacent to normal functional pituitary gland is radiation exposure to the pituitary, which frequently leads to the development of hypopituitarism. The authors describe a technique of pituitary transposition to reduce the radiation dose to the normal pituitary gland in cases of planned radiosurgical treatment of residual pituitary adenoma within the cavernous sinus. A sellar exploration for tumor resection is performed, the pituitary gland is transposed from the region of the cavernous sinus, and a fat and fascia graft is interposed between the normal pituitary gland and the residual tumor in the cavernous sinus. The residual tumor may then be treated with SRS. The increased distance between the normal pituitary gland and the residual tumor facilitates treatment of the tumor with radiosurgery and reduces radiation exposure to the normal pituitary gland.

Key Words • pituitary tumor • cavernous sinus • hypopituitarism • stereotactic radiosurgery

The most significant complication following conventional radiotherapy for residual or recurrent pituitary tumors is hypopituitarism, which requires life-long hormone replacement therapy.[1–3,7,17,24,28] Radiation-induced hypopituitarism is thought to result from direct damage to the pituitary gland and secondary damage to the hypothalamus. Up to 50% of patients with normal pituitary functions develop hypopituitarism within 5 to 20 years after undergoing conventional radiotherapy.[18,27] The time of onset is dose dependent, and its incidence increases with time from exposure.[19] Therefore, long-term follow-up study in these patients is necessary.

Radiosurgery has the potential to deliver high doses of radiation to the target lesion while reducing the dose to the surrounding normal structures. The proximity of the gland to the region of treatment, however, may carry the risk of developing hypopituitarism, even when SRS is applied. Stereotactic radiosurgery is being used more frequently in the treatment of pituitary tumors, both functioning and nonfunctioning, for residual tumor within the cavernous sinus.[10–12,14,15,22,25,26,29] The preliminary data regarding tumor control and normalization of hypersecretory syndromes after SRS appear promising.[2,9–17,21,22,25,26,29,30]

In cases in which there is cavernous sinus invasion and residual tumor is expected, the senior author (W.T.C.) has developed a technique for pituitary transposition ("hypophysopexy") in anticipation of postoperative radiosurgical treatment. This technique involves transposing the normal pituitary gland away from the cavernous sinus tumor and interposing a fat graft between the normal gland and the tumor in the cavernous sinus. This increases the distance between the normal pituitary gland and residual tumor to facilitate SRS treatment of the tumor, thereby reducing the effective biological dose to the normal pituitary gland. This reduction decreases the likelihood that hypopituitarism will develop. Although this technique has been described in the pituitary literature,[4] we detail it here for the neurosurgical readership and provide illustrative cases.

CLINICAL MATERIAL AND METHODS

Pituitary Transposition

A standard transsphenoidal approach (usually unilateral endonasal) is initially performed. Via an extended transsphenoidal approach, the osseous removal is then extended laterally toward the side of the cavernous sinus that in-

Abbreviations used in this paper: ACTH = adrenocorticotropic hormone; CA = carotid artery; MR = magnetic resonance; SRS = stereotactic radiosurgery.

volves tumor.[6,20] Maximum tumor resection is performed while leaving residual tumor in the cavernous sinus. Autologous fat and fascia lata are harvested from the patient's thigh in preparation for the pituitary transposition.

The normal pituitary gland is usually easily dissected from the adjacent recurrent tumor and displaced laterally away from the involved cavernous sinus. In addition, a margin of normal gland is removed from the tumor interface to ensure that none of the lesion is adherent to the normal gland before transposition. Fat is then interposed between the gland and the involved cavernous sinus to maintain the transposition. The closure then proceeds in a standard fashion, with fascia lata placed over the dural opening and additional fat graft within the sphenoid sinus to buttress the fascia.

We normally use autologous fat and fascia as graft material to prevent formation of cerebrospinal fluid fistulas.[5,6,20] The graft in these instances is contiguous with the standard fat–fascial graft placed in the sella and sphenoid sinus. Necrosis and shrinkage of the graft are expected in time and after radiosurgical treatment; this factor must be considered when undertaking fractionated treatments. If longer time periods for delivery of fractionated doses are considered, other more permanent materials, such as bone substitutes, may be better suited to maintain transposition of the gland.

CASE ILLUSTRATIONS

Case 1

History. This 16-year-old woman with acromegaly, treated at another institution, initially underwent an uncomplicated resection of her pituitary macroadenoma via a transsphenoidal route. A subtotal resection was performed, with residual tumor remaining in the left cavernous sinus. The patient remained clinically stable for more than 3 years while attending regular follow-up visits. She then noted some recurrence of the soft-tissue changes that she had experienced initially. The insulin-like growth factor–I level had continuously and rapidly elevated from 151 to 387 ng/ml over a 5-month period, and her serum growth hormone level had increased to 39 ng/ml. A repeated MR imaging study of the pituitary revealed residual tumor centered in the left cavernous sinus and in the enlarged sella just medial to it. Because of her recurrent progressive endocrinopathy and enlarging tumor, treatment was recommended. She refused medical treatment with a somatostatin analog; therefore, surgical removal and/or radiosurgical treatment of the remaining tumor was planned. The patient was young and unmarried; she was adamant about her desire that any planned treatment not affect her fertility.

Operation. A decision was made to reexplore the sella and parasellar region. The goals of surgery were maximum tumor resection and movement of the normal pituitary gland away from the residual tumor in preparation for radiosurgery. A standard microsurgical sublabial transsphenoidal approach was initially performed, as previously described.[6] Via an extended transsphenoidal route, additional bone was removed laterally to expose the tumor in the left lateral sella and cavernous sinus.[20] The normal pituitary gland was easily discernible from the residual pituitary adenoma. The tumor was dissected from the gland, and a 2-mm margin of normal lateral gland was removed to ensure its complete excision from the gland itself. The tumor was fibrous and difficult to dissect from the dura and CA. After extirpation of the medial aspect of the tumor, we decided to leave the remaining tumor in the cavernous sinus and to treat it radiosurgically to avoid the risk of CA injury and cavernous cranial neuropathy. A fat and fascia lata graft was harvested from the lateral thigh. The pituitary gland was then displaced to the right, and a fat graft was inserted to hold the gland away from the residual tumor and cavernous sinus (Fig. 1). Fascia lata and a fat graft were then placed over the dural opening to prevent formation of a cerebrospinal fluid fistula.

Postoperative Course and SRS. The postoperative course was uneventful, and the patient was discharged to home on the 3rd postoperative day. On postoperative Day 14 the residual tumor was treated with SRS without complication. Two 10-Gy fractions were delivered 4 weeks apart by using the Novalis shaped-beam system. Minimultileaf collimators were used to conform the treatment to the tumor while maintaining the dose to the brainstem and optic apparatus outside the 60% isodose region (Fig. 1). Transposition of the pituitary gland laterally with the fat graft enabled the radiation dose to the gland to be kept below the 50% isodose. At the time of her second treatment, some necrosis and retraction of the fat graft were already visible. Both treatments were uneventful. Ten months after SRS, her growth hormone and insulin-like growth factor–I levels had decreased to 2.1 ng/ml and 181 ng/ml, respectively. One year postoperatively, normal levels of other adenohypophysial hormones persisted (prolactin, 16 ng/ml) and her usual menstrual periods occurred approximately every 30 days. External ocular movements and facial sensation remain intact.

Case 2

History. This 42-year-old woman presented with Cushing disease secondary to an ACTH-secreting pituitary tumor that extended into the left cavernous sinus encasing the CA. Her ACTH level preoperatively was 93 pg/ml. A transsphenoidal resection was performed, and residual tumor, which invaded the left cavernous sinus, was left in place (Fig. 2). Postoperatively, elevated ACTH levels of 53 pg/ml persisted, and she suffered from malignant endocrinopathy. She was referred to an endocrinologist for adjuvant therapy; however, her follow-up status was suboptimal. A repeated MR imaging study 1 year later revealed recurrent tumor extending into the suprasellar cistern with radiographically demonstrated stable disease within the cavernous sinus.

Operation. Because of her persistent endocrinopathy (ACTH level 59 pg/ml and elevated 24-hour urine free cortisol) and recurrent tumor, we decided to reexplore the sella and parasellar regions, remove all accessible tumor, and transpose the pituitary gland in preparation for radiosurgical treatment of the cavernous sinus tumor. An endonasal transsphenoidal approach was used. Bone was removed laterally to expose the tumor in the left lateral sella and cavernous sinus. A plane was defined between the normal gland and the tumor. After removing the medial aspect of the tumor adjacent to the normal gland, a fat

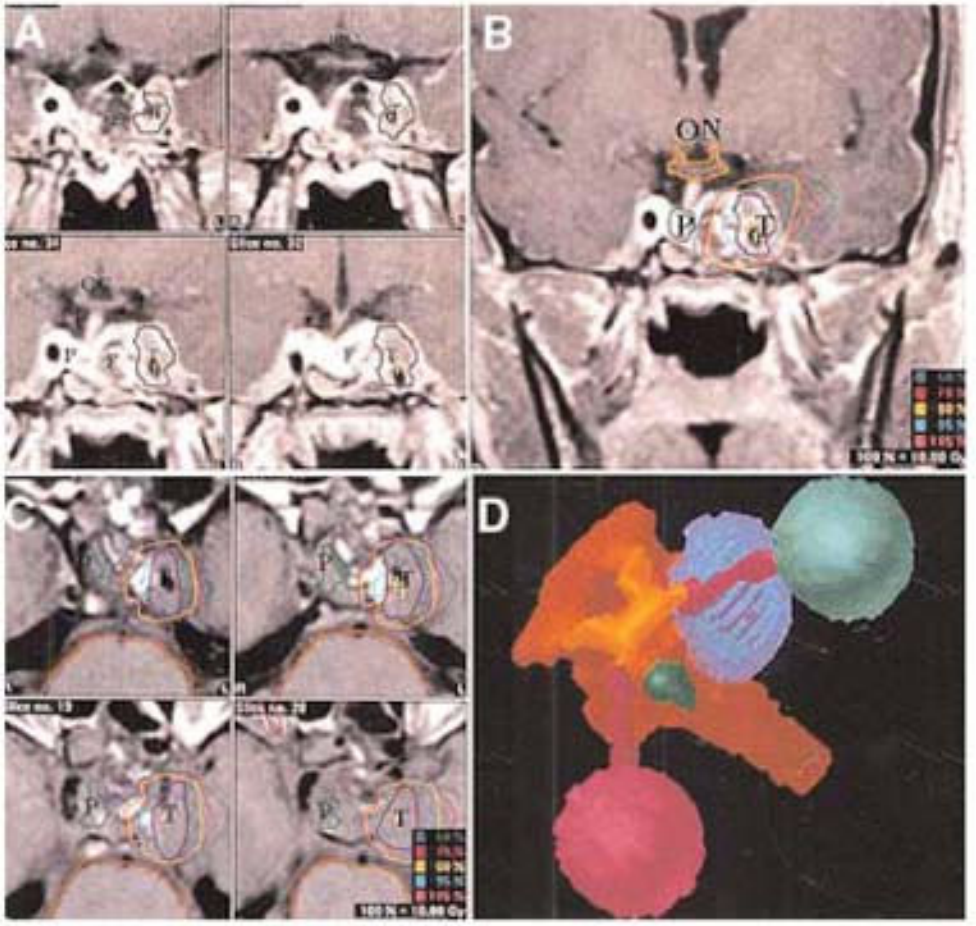

Fig. 1. Case 1. A: Coronal T_1-weighted Gd-enhanced MR images demonstrating the relationship of the cavernous sinus tumor (T), fat graft (F), optic chiasm (OC), and transposed pituitary gland (P). B and C: Isodose curves on coronal image demonstrating doses delivered to surrounding tissues on coronal (B) and axial images (C). Note lateral displacement of the gland by the interposed fat graft on coronal image (B). D: Diagram representing dosimetry target in relationship to brainstem and optic apparatus with transposed pituitary in green (from Couldwell, et al., 2002, with permission).

graft was interposed between the normal gland and the cavernous sinus tumor. A small piece of fascia lata was placed adjacent to the dural opening. The sphenoid sinus was then packed with fat to buttress the graft into position. A Marlex mesh pledget was fashioned to hold the fat within in the sphenoid sinus.

Postoperative Course and SRS. The postoperative course was uneventful, and the patient was discharged home on the 4th postoperative day. Two weeks later, she underwent intensity modulation–based radiosurgery for treatment of the cavernous sinus tumor; a single-fraction 20-Gy dose was prescribed at the 80% isodose line by using a plan of 22 fixed fields (Fig. 3). This strategy allowed better sparing of her left optic nerve, optic chiasm, left temporal lobe, and pituitary gland. The pituitary gland remained outside the 20% isodose line and received approximately 375 cGy. The patient tolerated the radiation well without complications. Cranial nerve functions remained intact. At 7 months after SRS, an endocrinological workup revealed no evidence of hypopituitarism. Her serum cortisol level was 10.1 μg/dl. An MR imaging study demonstrated no evidence of progression of residual tumor.

DISCUSSION

Stereotactic radiosurgery plays an increasing role in primary and adjuvant treatment of both functioning and non-

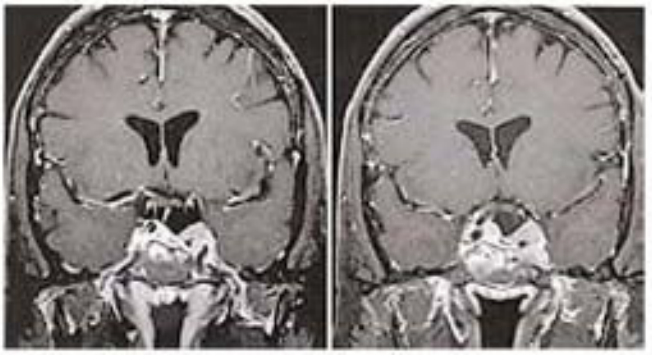

Fig. 2. Case 2. Postoperative coronal T_1-weighted Gd-enhanced MR images demonstrating residual pituitary tumor invading the left cavernous sinus and encasing CA. The pituitary gland is seen in the right sellar region.

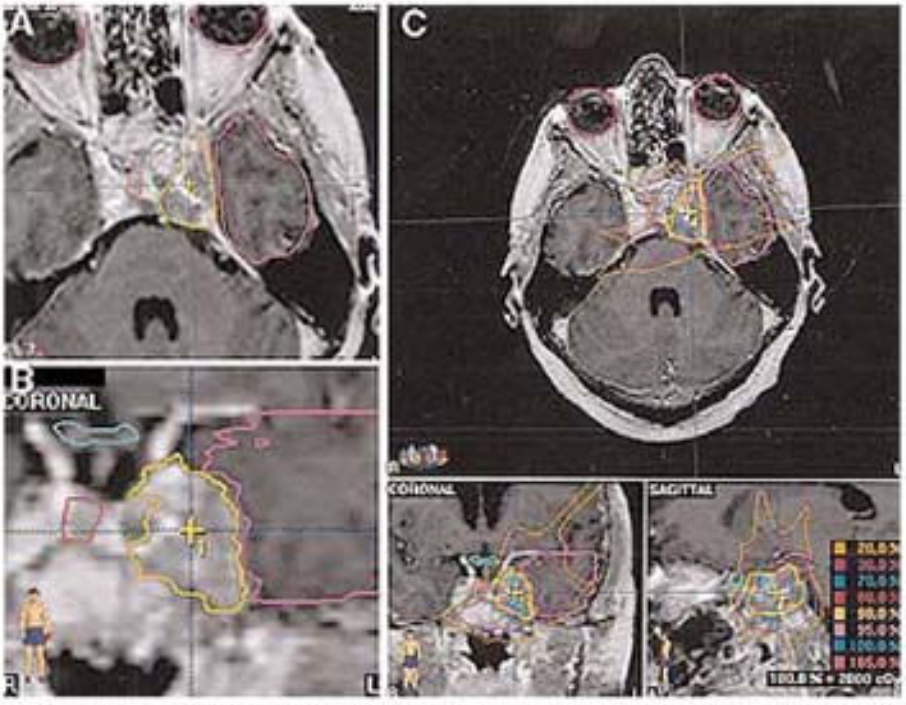

Fig. 3. Case 2. A and B: Intensity modulation–based radiosurgical plan (axial [A]; B, coronal [B] views). The T_1-weighted Gd-enhanced MR images demonstrate the relationship of the left temporal lobe *(purple)*, optic chiasm *(green)*, cavernous sinus tumor *(orange)*, transposed pituitary gland *(red)*, and fat graft (interposed between pituitary gland and cavernous sinus tumor). Note lateral displacement of the gland by the interposed fat graft on coronal image. C: Isodose curves depicting doses delivered to surrounding tissues. Note the relative sparing of the left optic nerve, optic chiasm, left temporal lobe, and pituitary gland. Both optic nerves and pituitary gland reside outside the 20% isodose line.

functioning pituitary tumors.[8–12,14,15,22,25,26,29,30] This method of delivering focal radiation is intuitively well suited to the treatment of localized tumors such as pituitary adenomas. The risk inherent in radiation-based treatments of pituitary adenomas, perhaps less with radiosurgery, is the development of hypopituitarism due to exposure of the adjacent pituitary gland.[18,19,27] In cases involving standard field irradiation treatments (200 cGy/fraction for a total dose of 5040 cGy) the risk of hypopituitarism is estimated to be 25% at 5 years and 50% at 10 years after treatment.[23] In SRS, a single dose of 10.9 Gy resulted in no clinical hypopituitarism at a short-term follow-up interval of 6 months to 2.6 years in patients with acromegaly in whom surgical therapy had failed.[15] No long-term follow-up studies of pituitary function after radiosurgical treatment of pituitary adenomas have been reported. Our technique for transposition of the pituitary gland is designed to increase the distance between the targeted tumor and the normal pituitary gland to reduce the effective biological dose to the latter structure. In doing so, the likelihood of inducing hypopituitarism is reduced, which is an important consideration when treating women of childbearing age.

CONCLUSIONS

We have described a pituitary transposition technique that may be used in highly selected cases of cavernous sinus tumor (especially functioning tumors) in patients in whom postoperative stereotactic radiotherapy or SRS is planned. This technique is designed to reduce radiation exposure of the normal gland.

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