Efficacy of Trans-septal Trans-sphenoidal Surgery in Correcting Visual Symptoms Caused by Hematogenous Metastases to the Sella and Pituitary Gland

Iman Feiz-Erfan, M.D.,^{1,2} Ganesh Rao, M.D.,² William L. White, M.D.,¹
and Ian E. McCutcheon, M.D.²

ABSTRACT

The rate of symptomatic improvement of visual symptoms associated with hematogenous metastases to the sella and pituitary was evaluated retrospectively in seven patients (five men, two women; mean age, 52.3 years) with primarily visual symptoms (diplopia alone in three, diplopia with blurred vision in one, blurred vision alone in one, loss of peripheral vision in one, and unilateral complete blindness in one). Symptom duration ranged from 0.5 to 2 months. The primary diseases were non-small cell lung cancer in two patients, renal cell carcinoma in two patients, prostate cancer in two patients, and medullary thyroid carcinoma in one patient. All patients had widespread metastatic disease. Three patients had a suprasellar tumoral component. One patient had a clival extension, and one patient had extension into the cavernous sinus. All underwent trans-sphenoidal surgery to correct visual symptoms. Gross total resection was achieved in three patients. Subtotal resections and a partial resection were performed in three patients and one patient, respectively. Surgical blood loss averaged 282 mL. One patient died from sepsis. Five patients developed complications (cerebrospinal fluid leakage in three, diabetes insipidus in two, anterior pituitary dysfunction in two, and colitis in one). At a mean follow-up of 15 months, three patients were alive. Visual symptoms improved in five patients and were unchanged in two. Trans-sphenoidal surgery helped improve visual symptoms in most patients. The morbidity rate was high and likely related to the locally destructive and extensive nature of the lesions in overall morbid patients with widespread metastatic disease. Unless

¹Division of Neurological Surgery, Barrow Neurological Institute, St. Joseph's Hospital and Medical Center, Phoenix, Arizona;
²Department of Neurosurgery, The University of Texas, M.D. Anderson Cancer Center, Houston, Texas.

Address for correspondence and reprint requests: Ian E. McCutcheon, M.D., Department of Neurosurgery, The University of Texas M.D. Anderson Cancer Center, PO Box 301402, Unit 442,

Houston, TX 77230-1402 (e-mail: imccutch@mdanderson.org).

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Received: May 19, 2006. Accepted: October 10, 2006.
Published online: January 4, 2008.

DOI 10.1055/s-2007-991105. ISSN 1531-5010.

nonoperative measures can provide equal results, however, this approach provides reasonable palliation.

KEYWORDS: Metastatic disease, pituitary gland, transnasal, sublabial, vision, sellar mass

Metastasis to the pituitary gland is found in 0.3% of unselected autopsies.¹ In autopsy studies of cancer cases, metastatic disease to the pituitary gland is a relatively common finding. In autopsy series of 1000 cases or more published in the English literature,^{1,2} the incidence has ranged from 1 to 1.8%. Based primarily on autopsy studies and literature review, the most frequent metastatic tumors to the pituitary gland and sella are breast and lung cancers.³⁻⁵

Metastases involving the sella and pituitary gland requiring surgical intervention are uncommon.⁶⁻¹⁰ Typically, symptoms include central diabetes insipidus (DI), anterior pituitary insufficiency, pain, headache, and visual disturbances.^{3,5,10-15} In fact, the presence of DI associated with a sellar mass is an important consideration that helps to differentiate a metastatic tumor in the sella from a pituitary adenoma.^{7,9} The most frequently reported symptom is DI. Visual deficits are reported in as many as 56% of cases.³

Surgical treatment of metastatic sellar tumors has been successful; visual symptoms tend to respond better than endocrinological symptoms.¹⁴ Trans-sphenoidal surgery for these lesions has been reported in as many as 3 to 16 cases from single institution series.^{3,6,8,14} However, details on specific outcomes related to visual symptoms after trans-sphenoidal resection of these lesions are limited.^{6,10} We retrospectively studied patients from two centers (Barrow Neurological Institute, Phoenix, Arizona, and The University of Texas, M.D. Anderson Cancer Center, Houston, Texas) to evaluate the rate of improvement of visual symptoms associated with hematogenous metastases to the sella and pituitary gland after a standard trans-septal transsphenoidal approach.

Treatment-related complications were also reviewed.

METHODS

Between 2000 and 2005, seven patients (five men, two women; mean age, 52.3 years) presented with primarily visual symptoms associated with metastases to the pituitary gland and sella: diplopia alone in three, diplopia with blurred vision in one, blurred vision alone in one, field cuts in one, and complete blindness in one. The duration of symptoms ranged from 0.5 to 2 months (mean, 1 month). At presentation and index surgery, all patients had widespread metastatic disease to other organs: bone in four, brain in three, lung in two, liver in one, and leptomeningeal spread in one. Endocrinological symptoms included one case of central DI and anterior pituitary deficiency. Preoperatively, one patient had panhypopituitarism from previous treatment of the sellar component; it was not a symptom of the metastatic tumor. The primary disease was non-small cell lung cancer in two patients, renal cell carcinoma in two patients, prostate cancer in two patients, and medullary thyroid carcinoma in one patient.

All patients' charts were reviewed retrospectively. Patients and their families were called to obtain the most recent follow-up information. One patient, who underwent resection of metastatic tumor to the pituitary gland via a trans-sphenoidal approach and who has previously been reported,¹⁶ was excluded because his primary presentation mode was profound endocrinological disturbance associated with minor visual symptomatology.

Three patients had a suprasellar tumoral component, one patient had a clival extension, and one patient had a cavernous sinus extension. All patients underwent a trans-septal trans-sphenoidal microscopic approach (transnasal approach in two and sublabial approach in five). All but one patient underwent trans-sphenoidal surgery as their primary treatment. One patient underwent a salvage procedure after a trans-sphenoidal procedure performed at an outside institution. One patient underwent a planned two-stage resection for significant suprasellar disease. The second stage was a transcranial approach.

RESULTS

Gross total resection was achieved in three patients. Subtotal (more than 95% of tumor resected) and partial (more than 50% of tumor resected) resections were performed in three patients and one patient, respectively (Table 1). Blood loss averaged 282 mL (range, 100 to 1000 mL).

One patient died within 30 days of surgery from sepsis likely related to a cerebrospinal fluid (CSF) leak that was initially managed successfully but then recurred. Five patients suffered from surgical complications (CSF leaks in three patients, DI in two patients, [one transient, one permanent], anterior pituitary dysfunction in two patients, and colitis in one patient). In all but one case, complications were managed successfully. The CSF leaks were treated with brief courses of lumbar spinal drainage. The two cases of DI were treated with hormonal supplementation. One case of central hypogonadism was treated with transient supplementation, and one case of anterior pituitary dysfunction was treated with permanent supplementation.

Postoperatively, visual symptoms improved in five patients (full recovery in two, significant improvement in two, and slight improvement in one) and were unchanged in two (one with complete unilateral visual loss, one with diplopia). The two patients who recovered fully had diplopia re-

lated to prostate cancer metastatic to the sella and pituitary gland. One had a tumoral extension to the clivus, and the other had an extension to the cavernous sinus. One of these patients underwent subtotal resection and the other had gross total resection of their metastases.

Hospital stays averaged 6.6 days (range, 3 to 15 days). All patients were discharged home. All patients except the one who died received adjuvant treatment. Six patients received radiation therapy after surgery (two of whom had stereotactic radiosurgery as the modality of radiation), two received chemotherapy, and two received hormonal therapy. No patients were lost to follow-up (mean follow-up, 15 months; range, 1 to 39 months). Three patients were alive at last follow-up.

ILLUSTRATIVE CASES

Case 1

A 55-year-old man sought treatment for new onset diplopia that had persisted for 2 weeks. Magnetic resonance imaging (MRI) showed a sellar tumor that extended into the right cavernous sinus. In 1996 he had been diagnosed with prostate cancer widely metastatic to multiple bony locations and had undergone treatment. In January 2005, the patient underwent a transnasal trans-sphenoidal resection of the sellar mass and its extension (Fig. 1). The histological diagnosis was metastatic prostate carcinoma. He was discharged home 3 days after surgery and underwent gamma knife radiosurgery to the sella and cavernous sinus followed by chemotherapy. He is alive and well 10 months after index surgery with no evidence of recurrence of the sellar disease. Postoperatively, his diplopia resolved completely.

Case 2

A 23-year-old woman with multiple endocrine neoplasia type IIb had a 1-month history of

Figure 1 Coronal T1-weighted magnetic resonance imaging (MRI) with contrast shows a metastatic intrasellar prostate carcinoma (arrow) that caused diplopia.

declining peripheral vision in the right eye, new onset DI, and anterior pituitary dysfunction associated with a sellar mass with suprasellar extension (Fig. 2). In 1990 the patient had been diagnosed with medullary thyroid carcinoma with metastatic spread to the lung, liver, and brain. The sellar and suprasellar mass was resected via a sublabial trans-sphenoidal approach. The histological diagnosis was metastatic medullary thyroid carcinoma. Her surgery was complicated by a CSF leak that required lumbar drainage. She was discharged home on hormonal supplementation for worsened panhypopituitarism. Her peripheral vision improved significantly. She died 2 months after surgery from progressive metastatic disease elsewhere in her body.

DISCUSSION

Symptom palliation in patients with metastatic cancer is an oncological imperative. In our seven

Figure 2 Coronal T1-weighted magnetic resonance imaging (MRI) with contrast shows a metastatic medullary thyroid cancer to the sella and pituitary gland that caused loss of peripheral vision.

patients with metastatic disease to the sella and pituitary gland, the primary goals of surgical intervention were to correct visual disturbances and to obtain tissue for diagnosis. These goals were achieved in 75% of the patients via the standard trans-septal trans-sphenoidal approach. However, the rate of surgical complications and death in this small group was high.

Complications were mostly related to CSF leaks, which were probably related to the locally infiltrative and destructive growth in the sella and suprasellar region and the tendency of such tumors to fuse with the diaphragma sellae. The leaks were effectively treated with short-term lumbar drainage and intraoperative packing with autologous fat placed in the sphenoid sinus and sella. However, the only surgical death, which was from sepsis, most likely resulted from a CSF leak that was initially controlled successfully.

Table 1 Clinical Summary of Patients with Visual Symptoms Treated with Trans-sphenoidal Surgery for Metastatic Disease to the Sella and Pituitary Gland

Case No.	Age/ Sex	Primary Tumor	Visual Symptom	Symptom Duration (mo)	Sellar Extension	Degree of Resection*	Complications	Visual Outcome	Length of Follow-up (mo)	Status
1	23/F	Medullary thyroid carcinoma	Loss of peripheral vision	1	Sella, suprasellar	Gross total	CSF leak, pan-hypopituitarism	Significant improvement	2	Died
2	55/M	Prostate cancer	Diplopia	0.5	Sella, cavernous sinus	Gross total	None	Full improvement	10	Alive
3	58/M	Renal cell carcinoma	Blurred vision, diplopia	0.5	Sella, suprasellar	Partial	Colitis	Significant improvement	7	Alive
4	73/M	Prostate cancer	Diplopia	1	Sella, clivus	Subtotal	None	Full improvement	39	Alive
5	71/F	Non-small cell lung cancer	Unilateral visual loss	1	Sella	Gross total	CSF leak, sepsis, death	Unchanged	1	Died
6	45/M	Renal cell carcinoma	Diplopia	0.75	Sella	Subtotal	Hypogonadism	Unchanged	38	Died
7	41/M	Non-small cell lung cancer	Blurred vision	2	Sella, suprasellar	Subtotal	CSF leak, DI	Mild improvement	8	Died

*Gross total resection = all visible tumor removed; subtotal resection = more than 95% of tumor removed; partial resection = more than 50% of tumor removed. CSF, cerebrospinal fluid; DI, diabetes insipidus.

We believe that the trans-sphenoidal route is better for accessing intrasellar pathology than basal frontotemporal approaches. If a carcinoma is associated with a significant suprasellar extension, a transcranial approach may be preferable to facilitate delicate dissection of the tumor from surrounding neurovascular tissue.¹⁷ Overall, however, we still favor the trans-sphenoidal route. A tumor's identity is often unknown preoperatively. Furthermore, despite a diagnosis of cancer and a sellar tumor, a pituitary adenoma can also be present.^{11,18} In fact, coexistence of a pituitary adenoma and metastatic carcinoma involving the pituitary gland has been reported, as has carcinoma metastatic to pituitary adenoma.^{11,19–21}

In our opinion the trans-sphenoidal route is superior to a transcranial approach for resection of a metastasis from the sella with preservation of the normal pituitary gland. Our study shows that trans-sphenoidal surgery effectively improves visual symptoms in most patients. We believe that the relatively brief interval from onset of visual symptom to surgery, which averaged 1 month, contributed to the overall good clinical response.

Improvement in visual symptoms after surgery for metastatic disease to the sella and pituitary gland is consistent with the literature.^{6,10,14} Among the presenting symptoms of metastatic disease to the sella and pituitary gland, visual symptoms best respond to surgical intervention, whereas endocrinological symptoms respond poorly.^{10,14} Therefore, surgery is a reasonable option for palliation of visual symptoms and for tissue diagnosis in patients with these metastatic cancers.³ This point is important because a significant proportion (29%) of these patients can expect to survive more than 3 years after index surgery, as outlined in our study. The range of survival is rather broad and extends from 1 to 39 months after index surgery. Potentially, the quality of life can be enhanced by correcting patients' presenting symptoms.^{10,14}

In the future, analysis of the outcome of nonsurgical treatments for patients with meta-

static disease to the pituitary gland and sella will help define which patients respond best to surgical therapy versus alternative strategies.^{12,13,22–27} Although radiosurgery or fractionated radiation as the primary treatment might avoid the complications associated with surgery and allow shorter hospitalizations, many patients with sellar metastasis cannot be treated with stereotactically focused single-fraction irradiation because such tumors are rarely detected before they have grown enough to abut the optic apparatus. Furthermore, radiotherapy does not provide the immediate decompression that these patients usually need.

It seems reasonable to ask whether stereotactic or fractionated radiotherapy to the sella, as a primary treatment for patients with visual complaints, is safer than surgery. Radiation has been reported as effective in treating ophthalmologic symptoms associated with parasellar or suprasellar metastatic disease.²⁸ Although data on this topic are scarce in patients with intrasellar metastatic lesions, some authors have suggested a potential role for radiation as a possible first-line treatment for this condition.^{24–26} We prefer to use it after surgery rather than as a front-line therapy. In certain scenarios, chemotherapy also may have an important role and may be useful in suppressing residual tumor as a postoperative adjuvant. Surgical resection of sellar metastasis is typically incomplete due to tumor adherence to the cavernous sinus walls or pituitary gland. For some metastatic carcinomas (e.g., breast, prostate), chemotherapy or hormonal therapy might palliate symptoms equally well, and surgery can thereby be avoided.^{23,27}

CONCLUSIONS

Trans-sphenoidal surgery effectively improved visual symptoms in most of our patients. However, the morbidity rate was high, likely reflecting the locally

destructive and extensive nature of the lesions in patients who were quite ill with widespread metastatic disease. Unless nonoperative measures can provide equal or better results, this approach provides reasonable palliation. Therefore, in patients suffering from hematogenous metastatic disease to the sella and pituitary gland who are primarily affected by visual symptoms, trans-sphenoidal surgery can and should be considered. If the patient is stable enough to undergo surgical intervention, good palliation associated with acceptable risks can be expected. Nonsurgical therapies, including radiation, chemotherapy, and hormonal therapy—or all three—remain treatment options for specific lesions and also may be useful in the postoperative setting.

ACKNOWLEDGMENT

The authors thank Leah M. Feiz-Erfan, R.N., for her support in preparing this manuscript.

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Commentary

The authors reviewed seven patients who underwent trans-septal and trans-sphenoidal surgery to correct visual symptoms caused by hematogenous metastases to the sella and pituitary gland. Gross total resection was achieved in a minority of patients. Therefore, the authors conclude that this type of surgery is appropriate for the treatment of visual symptoms, which improved in five of the seven patients. One patient died 30 days after surgery.

Given the population of patients, this outcome is not surprising. It underscores the issue that patients with advanced systemic malignancies are high surgical risks. Compared with patients with benign pituitary adenomas, these patients represent a different population. Therefore, they should provide appropriate informed consent before surgery. As the authors acknowledge, the complication rate is high: cerebrospinal fluid leakage in three patients, diabetes insipidus in two, anterior pituitary dysfunction in two, and one death related to surgery. In general, this surgical approach could be recommended for a select group

of patients with malignancies and significant visual impairment.

Randall W. Porter, M.D.¹

Commentary

This manuscript documents the efficacy of appropriately applied trans-sphenoidal decompression to reverse progressive visual loss in unfortunate patients who develop metastases to the pituitary. The authors' treatment improved vision in five of the seven patients. This information is important, and the authors are to be congratulated for their success despite the limited life expectancy of their patients. Interestingly, only two patients had diabetes insipidus at the time of presentation. The usual location for carcinomatous metastasis to the pituitary is the posterior lobe, and diabetes insipidus is an important part of the clinical presentation of most of these patients.

The authors emphasize that this surgery is not without risk. In fact, five patients developed complications. The most serious complication was spinal fluid leakage in one patient who required reoperation. Unfortunately, the patient developed meningitis and sepsis and died postoperatively.

It is important to realize that patients being treated for metastatic cancer who develop visual loss, headache, or diabetes insipidus may be harboring metastases to the pituitary region. In such cases, appropriate imaging studies and appropriate neurosurgical care may be indicated.

Edward R. Laws, Jr., M.D.¹

¹Interdisciplinary Skull Base Section, Barrow Neurological Institute, Phoenix, Arizona.

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¹UVA Department of Neurosurgery, UVA Health System, Charlottesville, Virginia.

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Tel: +1(212) 584-4662.

Published online: January 4, 2008.

DOI 10.1055/s-2007-991106. ISSN 1531-5010.

USA. Tel: +1(212) 584-4662.

Published online: January 4, 2008.

DOI 10.1055/s-2007-991107. ISSN 1531-5010.