Rare Infundibular Tumors: Clinical Presentation, Imaging Findings, and the Role of Endoscopic Endonasal Surgery in Their Management

Maria Koutourousiou¹ Paul A. Gardner¹ Julia K. Kofler² Juan C. Fernandez-Miranda¹
 Carl H. Snyderman³ L. Dade Lunsford¹

¹ Department of Neurological Surgery, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, United States

² Department of Pathology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, United States

³ Department of Otolaryngology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, United States

Address for correspondence and reprint requests Paul A. Gardner, MD, Department of Neurological Surgery, University of Pittsburgh School of Medicine, 200 Lothrop Street, Suite B400, Pittsburgh, PA 15213, United States (e-mail: gardpa@upmc.edu).

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Abstract

Background The spectrum of infundibular lesions is broad and distinct from sellar pathologies. In many cases, histology is needed to establish the correct diagnosis and determine the treatment approach.

Methods Medical files of eight patients with distinct infundibular tumors were reviewed. Histopathologically confirmed diagnosis included three pituitaryomas, three granular cell tumors, and two pilocytic astrocytomas.

Results Patients shared similar imaging findings and clinical symptoms, including visual impairment ($n = 5$), hypopituitarism ($n = 4$), and headache ($n = 4$); one patient presented with disseminated disease and symptoms from spinal metastases. All the pituitaryomas, two granular cell tumors, and one infundibular pilocytic astrocytoma case underwent endoscopic endonasal surgery; gross total resection was achieved in five patients, three developed postoperative diabetes insipidus, and two developed hypopituitarism. No recurrences were observed. One granular cell tumor patient was treated with gamma-knife radiosurgery after stereotactic biopsy; the tumor remained stable in size for over 9 years. The infundibular pilocytic astrocytoma patient who presented with spinal metastases received radiotherapy and systemic chemotherapy. The overall mean follow-up period was 25.1 months.

Conclusion Infundibular tumors are rare entities that represent a diagnostic challenge. Histopathological examination is essential for definitive diagnosis. Surgery, radiation therapy, and chemotherapy all have a role in the management of these tumors.

Keywords

- endoscopic endonasal approach
- granular cell tumor
- pilocytic astrocytoma
- pituitaryoma
- radiation therapy

Introduction

For most of the rare lesions that originate in the pituitary infundibulum (craniopharyngiomas excluded), treatment

protocols have not been established, and management of these cases remains challenging. The location of these tumors represents a dilemma for selection of the best surgical approach. Traditionally, the transcranial approach has been

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used for the majority of suprasellar masses. In selected cases, transsphenoidal surgery has been employed.^{1,2} The introduction of the endoscope in skull base surgery has recently expanded the indications of the endoscopic endonasal approach (EEA) for suprasellar tumor excision.^{3–5} Regardless of the approach, total tumor resection from such a demanding area is usually unsuccessful^{1,2,6} because of the vascular nature of tumors (as described for pituitaryomas and granular cell tumors), adhesions to the surrounding tissues, and infiltration of the pituitary infundibulum and even the hypothalamus. The presence of disseminated disease (in the case of astrocytomas) makes appropriate treatment selection even more complex. Tailored to individuals, surgery, radiation therapy or medical therapy can all have a role in the therapeutic approach of infundibular tumors.

In this series of eight infundibular tumors, we describe the presenting and imaging findings, as well as the histopathological characteristics identified in the tumor biopsy specimens. We present our therapeutic decisions, which were mainly based on the histopathological findings and the extent of the disease. We include a brief review of the three distinct pathologies identified in our series with emphasis on the treatment options.

Material and Methods

With approval by the Institutional Review Board, a retrospective review of patients with suprasellar lesions treated at the Department of Neurological Surgery between 2002 and 2010 was performed. In this study, we included discrete lesions primarily originating from the pituitary stalk that represented a preoperative diagnostic dilemma. Lesions involving the stalk by secondary extension, like sellar tumors with suprasellar extension or diffuse hypothalamic lesions, did not satisfy our inclusion criteria. Also, “common” suprasellar lesions like craniopharyngiomas or Rathke’s cleft cysts, which share more characteristic imaging findings, were excluded from this study. By applying these inclusion and exclusion criteria, eight distinct infundibular tumor cases were identified in our files.

Medical files were reviewed. Clinical presenting features, a consequence of local mass effect or invasion, were categorized into endocrine and neurological symptoms. Preoperative magnetic resonance imaging (MRI) was available for seven patients; one patient with a pacemaker had preoperative high-resolution contrast-enhanced computed tomographic (CT) scans of the hypothalamic-pituitary region. Preoperative imaging findings (tumor size, enhancement pattern) of each lesion were recorded. Posttreatment clinical information and imaging features were collected during the most recent follow-up visit of the patients to our clinics, except in one case where posttreatment information was obtained by telephone.

Treatment approach was selected according to tumor size and growth rate (as evaluated with serial imaging studies) and the presenting clinical symptoms of the patients (mainly, the evidence of visual impairment due to mass effect). With these criteria, surgical treatment (with the EEA) was offered

in six patients with the goal of maximum tumor removal. Intraoperative pathological consultation (with frozen sections) was not always diagnostic and did not change the treatment strategy. In the two other cases, surgery was used for tumor biopsy followed by treatment, which included gamma-knife radiosurgery, conventional radiation therapy, and systemic chemotherapy.

Diagnosis was established by histopathological examination of the infundibular specimen in all but one case, where the specimen from a spinal drop metastasis was available. All diagnostic material was reviewed for this retrospective study, and the initial diagnosis was confirmed in all cases. Histochemical and immunohistochemical studies were performed as part of the initial diagnostic work-up at the discretion of the case pathologist using standard techniques and the following primary antibodies: glial fibrillary acid protein (GFAP; predilute; Ventana, Tucson, Arizona, USA), S100 (1:500; Dako, Carpinteria, California, USA), epithelial membrane antigen (EMA; predilute; Cell Marque, Rocklin, California, USA), neurofilament (NF, clone 2F11; predilute; Ventana, USA), thyroid transcription factor 1 (TTF-1; 1:50; Dako), CD68 (clone KP-1; predilute; Ventana), Ki-67 (clone MIB-1, 1:100, Dako).

Results

Eight patients (five female, three male) with a median age of 41.4 years (range 25 to 63) were studied. Clinical presentation, histological diagnosis, treatment of the infundibular tumor, and outcome are summarized in ►Table 1.

Clinical Presentation

The most common clinical presentation of infundibular tumors was visual impairment (62.5%) followed by hypopituitarism (50%), headache (50%), and hydrocephalus in one case. We included one case that also had low back pain as a result of disseminated disease with drop metastases. ►Table 2 summarizes the clinical presentation according to the pathologies. Interestingly, none of the tumors that invaded the pituitary stalk presented with diabetes insipidus (DI). Hypothalamic-pituitary dysfunction was a common finding in every pathology group except pilocytic astrocytomas, where pituitary function was intact in all cases. Symptoms from disseminated disease occurred in one astrocytoma, whereas pituitaryomas and granular cell tumors always presented as a discrete, localized mass.

Imaging Findings

On neuroimaging studies, all the infundibular tumors in this series presented as distinct, solid masses that showed enhancement after contrast administration. The tumor size ranged from 8 to 25 mm with a rounded shape in most of the cases. In one case we observed a concomitant remote lesion, evidence of disease spread. The absence of high-intensity signal in the posterior pituitary lobe was noticed in one granular cell tumor case. There were no characteristic imaging features to differentiate diagnosis and a preoperative diagnosis based on imaging findings was not

Table 1 Clinical presentation with histological confirmed diagnosis, treatment, and outcome of eight patients with rare infundibular lesions

		Clinical presentation		Pathology	Management		Outcome			
Pt no.	Sex / age (yr)	Endocrine symptoms ^a	Neurological symptoms	Diagnosis	Treatment	Result	Postop condition ^a	Complications ^a	Recurrence	F/U (mo)
1	M/42	Hypopituitarism (LH/FSH)	Visual impairment	Pituitoma	Staged EEA	GTR	Normalized vision Hypopituitarism (LH/FSH)	Transient DI DVT	No	10
2	M/41	Hypopituitarism (GH, LH/FSH, TSH)	Headache; visual impairment	Pituitoma	EEA	GTR	Normalized vision Hypopituitarism (ACTH, GH, LH/FSH, TSH)	DI Hydrocephalus	No	14
3	F/63	None	Headache; visual impairment	Pituitoma	EEA	GTR	Normalized vision	DI Hypopituitarism (ACTH)	No	8
4	F/41	Hypopituitarism (TSH)	None	Granular cell tumor	Stereotactic biopsy/ gamma-knife	Stable tumor	Hypopituitarism (LH/FSH, TSH)	None	Tumor slightly increased in recent MRI	109
5	F/39	None	Headache; visual impairment	Granular cell tumor	EEA	Partial resection	Normalized vision	None	No	7
6	F/36	Hypopituitarism (ACTH, GH)	Visual impairment	Granular cell tumor	EEA	GTR	Normalized vision Hypopituitarism (ACTH, GH, LH/FSH, TSH)	DI	No	18
7	M/25	None	Hydrocephalus; low back pain	Pilocytic astrocytoma disseminated disease	Thoracic surgery for biopsy/ radio-radio-chemotherapy	N/A ^b	Occasional headaches	Flu-like symptoms post radio-chemotherapy	No	25
8	F/44	None	Headache	Pilocytic astrocytoma	EEA	GTR	Free of headaches	Transient DI Hypopituitarism (ACTH, TSH)	No	10

Abbreviations: ACTH, adrenocorticotrophic hormone; DI, diabetes insipidus; DVT, deep vein thrombosis; EEA, endoscopic endonasal approach; F, female; F/U, follow-up; GH, growth hormone; GTR, gross total resection; LH/FSH, luteinizing hormone/follicle-stimulating hormone; M, male; MRI, magnetic resonance imaging; PT no., patient number; TSH, thyroid stimulating hormone.

^aThe specific hormone deficiency is given in parentheses.

^bFollow-up obtained via telephone and although patient has regular MRI every 6 months and no complaints, MRIs were not available to us.

Table 2 Clinical presentation of infundibular tumors

	Pituicytomas (<i>n</i> = 3)	Granular cell tumors (<i>n</i> = 3)	Pilocytic astrocytoma (<i>n</i> = 2)	Total (<i>n</i> = 8)
Headache	2	1	1	4
Visual impairment	3	2	0	5
Hypopituitarism	2	2	0	4
Hydrocephalus	0	0	1	1
Low back pain	0	0	1 ^a	1 ^a

^aDisseminated disease.

feasible. ► **Table 3** summarizes the radiographic findings of the infundibular tumors.

Histopathological Diagnosis

Histopathological examination revealed three distinct diagnostic entities: pituicytoma (*n* = 3), granular cell tumor (*n* = 3), and pilocytic astrocytoma (*n* = 1). In one case with an intradural spinal lesion, biopsy of the spinal mass revealed a low-grade glial neoplasm with exuberant reactive leptomeningeal proliferation. The microscopic features were not sufficient for a definitive diagnosis, but a pilocytic astrocytoma was favored and fit the remaining clinical picture.

Pituicytomas were moderately cellular spindle cell neoplasms with nuclear positivity for thyroid transcription factor-1 (TTF-1).⁷ Granular cell tumors were composed of large polygonal cells with periodic acid-Schiff (PAS)-positive granular eosinophilic cytoplasm. Both neoplasms exhibited nuclear and cytoplasmic staining for S100, but absent or only focally present glial fibrillary acidic protein (GFAP) reactivity. In all granular cell tumors and pituicytomas, Ki-67 proliferation index was less than 1 to 2%.

The confirmed case of pilocytic astrocytoma was composed of bipolar piloid glial cells with prominent nuclear palisading. Scattered hyaline bodies but no eosinophilic granular bodies or Rosenthal fibers were seen. The tumor cells were strongly labeled with GFAP, and the Ki-67 proliferation index was < 1%. TTF-1 was weakly positive in rare tumor cell nuclei but negative in the vast majority of cells.

Treatment and Outcome

At the time of surgery, the diagnoses were unknown. Surgery, with the EEA, was planned for six patients given the visual deterioration they experienced or tumor growth as evident in serial MRIs. The goal of surgery was to decompress the optic chiasm, obtain diagnosis, relieve/prevent symptoms, and provide maximum possible safe tumor resection. The intraoperative pathology consultations (smears or frozen sections) were not always accurate, highlighting the diagnostic challenge of these lesions. However, the intraoperative pathological findings did not significantly affect the surgical goal of gross total resection (GTR) whenever the surgical findings allowed. None of the patients who underwent EEA had a

Table 3 Imaging findings in 8 patients with infundibular tumors

Pt no	Diagnosis	Imaging findings					
		Size (mm)	Contrast Enhancement	MRI T1WI	MRI T2WI	CT	Bright spot of neurohypophysis
1	Pituicytoma	20 × 20	Solid - Homogeneously	Isointense	Isointense	n/a	+
2	Pituicytoma	18 × 16	Solid - Homogeneously	n/a	n/a	Isodense	n/a
3	Pituicytoma	25 × 25	Solid - Heterogeneously	Isointense	Hyperintense	Isodense	+
4	Granular cell tumor	19 × 17	Solid - Homogeneously	Isointense	Iso/hypointense	n/a	–
5	Granular cell tumor	16 × 15	Solid - Homogeneously	Isointense	Iso/hypointense	n/a	+
6	Granular cell tumor	15 × 13	Solid - Homogeneously	Isointense	Iso/hypointense	n/a	+
7	Pilocytic astrocytoma ^a	11 × 8	Solid - Homogeneously	Iso/hypointense	Hyperintense	Isodense	+
8	Pilocytic astrocytoma	11 × 11	Solid - Homogeneously	Isointense	Isointense	n/a	+

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; n/a, not available; PT no, patient number; T1WI, T1-weighted image; T2WI, T2-weighted image. Note: The signal intensities were compared with cerebral cortex.

^aDisseminated disease.

postoperative cerebrospinal fluid (CSF) leak. In patient 4 with a slow-growing tumor and intact vision, we elected to stereotactically biopsy and later performed radiosurgery; a single 4 mm isocenter was used with 10 Gy at the 45% isodose; maximum dose was 22.22 Gy. Patient 7, who presented with disseminated disease, was treated with radiotherapy and systemic chemotherapy after biopsy of the remote spinal metastasis.

All the patients with pituicytoma underwent EEA, in one case staged, and GTR of the tumor was achieved in every case (►Fig. 1). In two instances, transposition of the pituitary

gland was considered necessary to facilitate access to the retroinfundibular aspect of the tumor. Preexisting hypopituitarism remained stable in two patients and vision was normalized in every case. One patient developed new hypopituitarism, one experienced transient DI and two permanent DI requiring treatment with desmopressin. One patient with postoperative deep vein thrombosis (DVT) was treated with anticoagulants without further complications. Postoperative hydrocephalus in one patient was resolved with the placement of a ventriculoperitoneal (VP) shunt; since there was no evidence of residual tumor after surgery, we assume that

Fig. 1 Pituicytomas. Patient 1: preop midline magnetic resonance imaging (MRI) (left) showing a rounded suprasellar mass and postop (right) MRI after endoscopic endonasal approach (EEA) and gross total resection of the tumor (A). Patient 2: preop (left) and postop (right) computed tomography (CT) demonstrating the gross total resection of the pituicytoma (B). Patient 3: preop midline MRI (left) illustrating a heterogeneous suprasellar tumor which was totally resected with the EEA as showed on the postop MRI (right; C).

blood products caused an obstruction at the level of the subarachnoid space, resulting in postoperative hydrocephalus in this patient. During a 10.7-month follow-up, none of the patients experienced tumor recurrence.

Among the patients with granular cell tumor, two underwent EEA and one underwent radiosurgery (►Fig. 2). GTR was achieved in one patient with preexisting hypopituitarism who developed postoperative DI. In the other surgical case, given the intact pituitary function, we proceeded with a less aggressive subtotal tumor resection with the aim of optic

nerve decompression. The patient remained endocrinologically intact. None of these patients showed tumor recurrence during the follow-up period (18 and 7 months, respectively). The patient who was treated with gamma-knife radiosurgery after stereotactic biopsy of the tumor remained clinically stable and, although the tumor failed to shrink, tumor size remained unchanged during the 109-month follow-up; in the most recent MRI, there is evidence of a slight increase in tumor volume, and the patient is undergoing close follow-up.

Fig. 2 Granular cell tumors. Patient 4: magnetic resonance imaging (MRI) after stereotactic biopsy of the midline suprasellar mass (left); the patient was treated with gamma-knife radiosurgery and the tumor remained stable in size for over 9 years. In the most recent MRI (right), a slight increase in tumor volume had been observed (A). Patient 5: preop midline MRI (left) showing a rounded suprasellar mass; a less aggressive surgical resection with the endoscopic endonasal approach was employed and subtotal tumor resection was achieved (right) with preservation of pituitary function (B). Patient 6: preop (left) and postop (right) midline MRIs showing the location of the tumor and the gross total resection following endoscopic endonasal surgery (C).

Fig. 3 Infundibular pilocytic astrocytoma. Patient 8: preop midline magnetic resonance imaging (left) illustrating the solid infundibular mass; the patient underwent endoscopic endonasal approach and gross total resection of the tumor was achieved (right). The increased linear enhancement over the sellar fossa and the planum represents the vascularized nasoseptal mucosal flap which is used for reconstruction.

The patient with a discrete pilocytic astrocytoma originating from the infundibulum showed tumor growth on serial MRIs, and he underwent EEA with transposition of the pituitary gland; GTR was achieved and adjuvant treatment was not considered necessary (—Fig. 3). The patient developed transient postoperative DI (resolved after 9 months) and hypopituitarism and receives hormonal replacement therapy. The other case (patient 7) presented with concomitant multiple lesions along the thoracic spine (—Fig. 4). A VP shunt was placed to relieve symptoms of hydrocephalus. The diagnosis was confirmed with biopsy of the spinal tumor, which showed a “low-grade glial neoplasm with exuberant reactive leptomeningeal reaction”; based on the clinical history and histopathologic findings, this intradural spinal tumor was considered to represent a CSF “drop” metastasis of a low-grade glial neoplasm consistent with pilocytic astrocytoma. Given the disseminated disease at presentation, the patient was treated with radiotherapy and systemic chemotherapy. His follow-up was obtained by telephone and although he claims to be free of symptoms or recurrence, his posttreatment imaging studies were not available to us.

Discussion

The noncharacteristic clinical and imaging findings of infundibular tumors represent a diagnostic challenge resulting in treatment dilemma. Biopsy of these lesions is an important step to define diagnosis and proceed to the recommended therapy. However, the rarity of these tumors and the consequently limited knowledge of their natural history and response to adjuvant therapies (radiotherapy, chemotherapy) results in lack of optimal treatment protocols. The incidence of visual deterioration due to mass effect of the tumor makes the surgical approach for decompression a reasonable option. The increased indications of the EEA have recently expanded to suprasellar tumors.^{3–5} New reconstruction techniques, like the vascularized nasoseptal flap,⁸ have resulted in the absence of postoperative CSF leak in every patient of this series who underwent EEA. Systemic chemotherapy for disseminated disease in case of astrocytomas has been accepted as the ultimate treatment option.^{9,10} Radiotherapy can be applied in cases of slow-growing tumors with intact vision at presentation or as adjuvant therapy after subtotal tumor resection.

Fig. 4 Infundibular pilocytic astrocytoma, disseminated disease. Patient 7: midline magnetic resonance imaging (MRI) of the head (left) shows an infundibular mass measuring 11 mm in its maximum diameter; spinal MRI (right) illustrating concomitant lesions of the thoracic spine (arrows) which were considered to represent cerebrospinal fluid “drop” metastases.

Gamma-knife radiosurgery is not contraindicated in cases of tumor contiguity to the optic apparatus, and the success of treatment is related to the technology used, the tumor edge dose delivered, and the conformality and selectivity of the computer dose plan; the target histology may also be important in determining the optimal treatment dose. However, the efficacy of radiotherapy for residual pituicytomas and granular cell tumors has not been studied, thus it is not proven that a less aggressive surgical technique combined with postoperative radiation therapy is favorable over a GTR of the lesion. On the other hand, the high rate of postoperative DI after GTR in our series combined with apparent good response to radiation therapy increases the dilemma of whether a more aggressive approach for GTR is favorable over a subtotal resection with preservation of the infundibular function. Certainly, initial observation of tumors without endocrine or neural compromise is recommended given the slow growth of the vast majority of them.

Pituicytomas

Pituicytoma is defined as a solid, circumscribed, low-grade (World Health Organization [WHO] grade I) spindle cell astrocytic tumor arising in adults from pituicytes in the posterior pituitary gland and/or stalk.¹¹ Historically, the term *pituicytoma* has been used for various tumors in the suprasellar region or posterior pituitary, but in the recent edition of the WHO Classification of the Nervous System,¹² pituicytoma has been added as a distinct and defined entity to the section of gliomas, and new information is introduced reflecting both the recognition and a better understanding of its neoplastic behavior.¹¹ The clinical presentation is often a result of mass effect, with pituitary insufficiency, visual impairment, and headache being the most common symptoms.^{1,13} Although pituicytomas originate in the neurohypophysis and/or infundibulum, DI has rarely been reported as a presenting clinical finding. The neuroimaging features of the tumor are not distinctive from other lesions of the region. On MRI, they are isointense on T1-weighted images and hyperintense on T2-weighted images, with bright enhancement after contrast administration, which probably correlates with their increased vascularity.^{14,15} These MRI characteristics were found in our two patients who underwent preoperative MRI.

In clinical series, the pituicytoma remains an extraordinarily rare tumor of the neurohypophysis and, according to the latest reviews, less than 40 cases have been reported.^{1,16} Due to the rarity of the tumor, little is known about its natural history and optimal management. However, since subtotal excision has been associated with tumor recurrence, total tumor resection appears to be the mainstay of treatment.^{1,13,17} As reported previously,^{1,17,18} pituicytomas are much more vascular than any other typical suprasellar lesion, which was true in two out of three cases in our series. Complete resection is often limited by bleeding or by location when the pituicytoma involves the stalk, resulting in unsuccessful total excision in more than 50% of the published cases.¹

We achieved GTR of pituicytomas in every case with endoscopic endonasal surgery (EES). EES facilitates direct

access to the tumor without manipulations of the optic apparatus and good control of the tumor's arterial supply, which is usually a branch of the superior hypophyseal artery (SHA) (►Fig. 5). Coagulation of the feeding branch of the SHA, which is located directly under the optic chiasm, is the best way to control disastrous intraoperative bleeding from vascular tumors, and this is facilitated through the endonasal corridor. In the challenging case of suprasellar tumors with retroinfundibular extension, we combine EEA with pituitary transposition, which enables access to the posteroinferior tumor margins and may provide some chance for hormone recovery long term.¹⁹ Although the pituitary infundibulum was anatomically preserved in every case in our series, its function was lost in two cases (►Fig. 6). The origin of the

Fig. 5 Endoscopic resection of a pituicytoma (patient 2). Upper: intraoperative view with a 0-degree endoscope showing the pituitary gland (PG) and the tumor (Tu) after opening of the suprasellar dura (D). Initial tumor debulking has taken place in the midline, in between the pituitary stalk (S), which was split in the midline by the tumor. The bone remover over the sella and tuberculum sella has been extended laterally exposing both cavernous sinuses (CS). Lower: intraoperative view during tumor (Tu) removal with the two suctions technique. The PG is protected with the intact dura. At the superior aspect of the tumor, the right SHA ([R]SHA) is identified lying just beneath the optic chiasm (not shown).

Fig. 6 Intraoperative view of the third ventricle opening with a 0-degree endoscope after total tumor resection (patient 2). The tumor was extended up to the anterior recess of the third ventricle (3rd V), which was opened to achieve complete resection. The optic chiasm (OCh) is totally decompressed. The pituitary gland (PG) is hung from the preserved split stalk (S). Regardless of the anatomical preservation of the infundibulum, its function was lost.

lesions from the pituitary stalk makes the manipulation of the stalk inevitable, and this may contribute to postoperative hypopituitarism and DI. The main vascular concern when dealing with tumors of the interpeduncular cistern is control of the posterior cerebral arteries (PCAs), which are located at the posterior margins of the lesion and, therefore, are difficult to visualize. The use of angled endoscopes and pituitary transposition is essential for safe visualization and dissection of the tumor from the surrounding vital neurovascular structures.

Considering that GTR is the treatment of choice for pituitaryomas, it remains controversial which is the best surgical approach given the potential endocrine and neurologic deficits. Among 27 pituitaryoma patients who underwent surgery for their lesion, in only 12 cases (44%) GTR was achieved regardless of the selected surgical approach.¹ Although complications were not always mentioned, in two cases postoperative DI developed after GTR.¹ As expected, a more aggressive technique to facilitate GTR is associated with higher risk of complications due to manipulation of the stalk, which was evident in our cases. Interestingly, very few surgical complications have been reported (4 cases of transient DI, 1 of hypopituitarism, and 1 of transient hemiparesis).¹ One could expect higher rates of stalk dysfunction, even transient, after surgery for “infundibulomas.”

Still, the rarity of the pituitaryomas prevents the establishment of management protocols. The efficacy of radiotherapy for residual tumors has not been studied, thus it is not proven that a less aggressive surgical technique combined with postoperative radiation therapy is favorable over a GTR of the lesion.

Granular Cell Tumors

Granular cell tumors of the neurohypophysis or the pituitary stalk are usually slow-growing benign tumors that, like

pituitaryomas, derive from pituitary cells and are thought to be related tumors^{17,20} with distinct histopathological appearances.^{17,21} Given their common origin, granular cell tumors and pituitaryomas are highly location-specific and share similar clinical and neuroimaging features. Symptoms are typically chronic and progressive, resulting from compression of surrounding structures.^{2,20} Like in pituitaryomas, DI is an unusual finding despite the site of origin of these tumors.^{2,20} Granular cell tumors lack characteristic imaging findings to differentiate them from other lesion of the sellar/suprasellar region. MRI shows masses that are isointense to the brain on T1- and T2-weighted sequences, with homogenous or heterogeneous moderate to intense contrast enhancement.^{2,20} Our cases share the same clinical and imaging characteristics described in the literature. We also observed absence of the high-intensity signal in the posterior pituitary lobe in patient 4 without clinical evidence of DI (a finding well documented for infundibular germinomas). We do not know if this is an incidental finding or if it has been caused by a “damming-up” phenomenon from stalk compression leading to accumulation of neurosecretory vesicles containing vasopressin in the pituitary stalk. This results in high intensity of the stalk, absence of bright spot in the neurohypophysis, and preservation of the hypothalamic-neurohypophyseal function.²²

Approximately 60 cases of symptomatic granular cell tumors within the neurohypophysis/stalk have been reported to date^{2,23}; however, their prevalence is higher in autopsies,^{24,25} which supports their indolence and rarity of symptoms.²⁶ There is a characteristic female predominance, which was also true in our series. According to the most recent review by Cohen et al,² 44 of the 61 published granular cell tumor cases underwent surgery and the rest were treated with radiation therapy. Among the surgical cases, in 13 (29.5%) GTR was achieved regardless of approach (craniotomy or transsphenoidal surgery).² The firm and vascular nature of granular cell tumors along with the lack of obvious dissection plane between the tumor and normal brain were considered the main limitations for GTR.^{2,23} In our cases, we did not experience excessive or uncontrolled intraoperative bleeding.

We employed EES in two firm, granular cell tumor cases, with GTR achieved in one case. In patient 5 we performed cytoreductive surgery to maintain postoperative pituitary function. None of our patients experienced postoperative visual deterioration, which was a concern in previous published cases, with an incidence as high as 45%.² In the same series,² postoperative DI and hypopituitarism developed in 36% and were correlated with the surgical aggressiveness in attempting GTR. Injury to the stalk during complete removal of infundibular tumors is almost inevitable regardless of the selected surgical approach.

Again, the most favorable treatment for granular cell tumors has to be established. Although the natural history of granular cell tumors is poorly understood, they are typically considered benign, slow-growing tumors that rarely become symptomatic. As a result, observation of asymptomatic tumors is highly recommended and subtotal tumor resection with preservation of infundibular function might be considered a more advantageous approach.

In light of the slow growth of granular cell tumors, the role of radiation therapy in their treatment remains controversial.² In their review of the literature, Schaller et al concluded that radiation therapy alone may provide no benefits.²³ In our experience, the patient who was treated with gamma-knife radiosurgery showed stable tumor size for 109 months and only recently a slight increase in tumor size was observed (patient 4). At present, the small number of patients treated with radiotherapy and the limited follow-up period preclude any definite conclusions regarding the use of radiotherapy as primary or adjuvant therapy in the treatment of granular cell tumors.

Suprasellar Pilocytic Astrocytomas

Pilocytic astrocytoma is a characteristically slow-growing, well-circumscribed WHO grade I glioma accounting for 2.3% of all reported brain tumors.¹² Although the most common type of brain tumors in the pediatric population, pilocytic astrocytoma is quite rare in adults.²⁷ Pilocytic astrocytoma can occur anywhere along the neuraxis, including the suprasellar region. In the hypothalamic/chiasmatic region, the clinical presentation is a result of mass effect or the rare but characteristic in children diencephalic syndrome (failure to thrive, decreased visual field, nystagmus, hyperactivity, euphoria, hypoglycemia).²⁸ On MRI, pilocytic astrocytoma is typically isointense to hypointense relative to normal brain with T1-weighted images and hyperintense in T2-weighted images with intense enhancement after contrast administration.²⁹ When occurring in the hypothalamic/chiasmatic region, they may have more intense homogeneous enhancement and homogeneous hyperintensity on T2-weighted images.³⁰

Pilocytic astrocytoma is generally considered a benign tumor with an excellent prognosis following complete surgical resection (which is the treatment of choice). In such cases survival rates approach 100%.³¹ The EEA can facilitate GTR of pilocytic astrocytomas originating solely from the infundibulum, as was evident with patient 8. As seen with our experience with pituitaryomas and granular cell tumors, manipulation of the stalk, which is already invaded by tumor, greatly increases the risk of postoperative dysfunction. It is well established that the extent of tumor resection is a critical determinant of prognosis and that patients who undergo partial resection of low-grade gliomas have shorter progression-free survival times than do patients who undergo GTR.⁶ On the other hand, studies demonstrated that even patients who undergo partial resection of pilocytic astrocytomas have excellent long-term prognoses.³² Therefore, as with other infundibular tumors, aggressiveness of resection should be tempered by potential risk.

Pilocytic astrocytomas rarely exhibit an aggressive course. Leptomeningeal dissemination is a rare phenomenon that can either present years after the initial brain tumor diagnosis (75% of the cases) or synchronously (25%).²⁷ Tumor seeding due to leptomeningeal dissemination is thought to occur when tumor cells are in close proximity to CSF spaces. This is seen specifically in pilocytic astrocytomas of the hypothalamic-chiasmatic region, which have a 23-times higher risk of

dissemination than pilocytic astrocytomas in any other area.³³ We believe that this was the pathophysiology of the disease in patient 7 who presented with spinal drop metastases. In these cases of unresectable lesions or leptomeningeal spread, radiation therapy and chemotherapy are recommended.^{9,10}

Conclusion

Discrete, solid tumors originating from the pituitary infundibulum are rare entities without characteristic clinical or radiographic findings to enable an accurate diagnosis without biopsy. Lack of treatment protocols for most of these "rare" tumors makes their management a real challenge. This is especially true for the treatment of pituitaryomas and granular cell tumors of the pituitary stalk, as their rarity results in limited knowledge on their natural history and response to therapies. EES can be employed both for biopsy and resection of symptomatic or progressive infundibular tumors. However, surgeons must be aware of the potential complications when operating on potentially slow-growing tumors that infiltrate or originate from the pituitary stalk. The incidence of metastasis from suprasellar astrocytomas is an important factor of outcome, treatment selection and initial evaluation. In these cases, radiation therapy and chemotherapy can be used either as initial or adjuvant treatment. In any case, treatment must be individualized according to the histological diagnosis and the general condition of the patient. Long term follow up is essential to evaluate the optimal treatment for each lesion.

References

- 1 Wolfe SQ, Bruce J, Morcos JJ. Pituitaryoma: case report. *Neurosurgery* 2008;63:E173–E174, discussion E174
- 2 Cohen-Gadol AA, Pichelmann MA, Link MJ, et al. Granular cell tumor of the sellar and suprasellar region: clinicopathologic study of 11 cases and literature review. *Mayo Clin Proc* 2003;78:567–573
- 3 Halves E, Bushe K-A. Transsphenoidal operation on craniopharyngiomas with extrasellar extensions. The advantage of the operating endoscope [proceedings]. *Acta Neurochir Suppl (Wien)* 1979;28:362
- 4 Cappabianca P, Cavallo LM, Esposito F, De Divitiis O, Messina A, De Divitiis E. Extended endoscopic endonasal approach to the midline skull base: the evolving role of transsphenoidal surgery. *Adv Tech Stand Neurosurg* 2008;33:151–199
- 5 Kassam A, Snyderman CH, Mintz A, Gardner P, Carrau RL. Expanded endonasal approach: the rostrocaudal axis. Part I. Crista galli to the sella turcica. *Neurosurg Focus* 2005;19:E3
- 6 Komotar RJ, Burger PC, Carson BS, et al. Pilocytic and pilomyxoid hypothalamic/chiasmatic astrocytomas. *Neurosurgery* 2004;54:72–79, discussion 79–80
- 7 Lee EB, Tihan T, Scheithauer BW, Zhang PJ, Gonatas NK. Thyroid transcription factor 1 expression in sellar tumors: a histogenetic marker? *J Neuropathol Exp Neurol* 2009;68:482–488
- 8 Hadad G, Bassagasteguy L, Carrau RL, et al. A novel reconstructive technique after endoscopic expanded endonasal approaches: vascular pedicle nasoseptal flap. *Laryngoscope* 2006;116:1882–1886
- 9 Nishio S, Morioka T, Takeshita I, et al. Chemotherapy for progressive pilocytic astrocytomas in the chiasmo-hypothalamic regions. *Clin Neurol Neurosurg* 1995;97:300–306

- 10 Aryan HE, Meltzer HS, Lu DC, Ozgur BM, Levy ML, Bruce DA. Management of pilocytic astrocytoma with diffuse leptomeningeal spread: two cases and review of the literature. *Childs Nerv Syst* 2005;21:477–481
- 11 Wesseling P, Brat DJ, Fuller GN. Pituicytoma. In: Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, eds. *WHO classification of Tumours of the Central Nervous System*. IARC: Lyon; 2007
- 12 Louis DN, Ohgaki H, Wiestler OD, et al. The 2007 WHO classification of tumours of the central nervous system. *Acta Neuropathol* 2007;114:97–109
- 13 Brat DJ, Scheithauer BW, Staugaitis SM, Holtzman RN, Morgello S, Burger PC. Pituicytoma: a distinctive low-grade glioma of the neurohypophysis. *Am J Surg Pathol* 2000;24:362–368
- 14 Katsuta T, Inoue T, Nakagaki H, Takeshita M, Morimoto K, Iwaki T. Distinctions between pituicytoma and ordinary pilocytic astrocytoma. Case report. *J Neurosurg* 2003;98:404–406
- 15 Hurley TR, D'Angelo CM, Clasen RA, Wilkinson SB, Passavoy RD. Magnetic resonance imaging and pathological analysis of a pituicytoma: case report. *Neurosurgery* 1994;35:314–317, discussion 317
- 16 Hammoud DA, Munter FM, Brat DJ, Pomper MG. Magnetic resonance imaging features of pituicytomas: analysis of 10 cases. *J Comput Assist Tomogr* 2010;34:757–761
- 17 Ulm AJ, Yachnis AT, Brat DJ, Rhoton AL Jr. Pituicytoma: report of two cases and clues regarding histogenesis. *Neurosurgery* 2004;54:753–757, discussion 757–758
- 18 Benveniste RJ, Purohit D, Byun H. Pituicytoma presenting with spontaneous hemorrhage. *Pituitary* 2006;9:53–58
- 19 Kassam AB, Prevedello DM, Thomas A, et al. Endoscopic endonasal pituitary transposition for a transsellar approach to the interpeduncular cistern. *Neurosurgery* 2008;62(3, Suppl 1): 57–72, discussion 72–74
- 20 Menon G, Easwer HV, Radhakrishnan VV, Nair S. Symptomatic granular cell tumour of the pituitary. *Br J Neurosurg* 2008;22: 126–130
- 21 Lee CC, Liu CH, Wei CP, How SW. Symptomatic granular cell tumor of the neurohypophysis. *J Formos Med Assoc* 2004;103:58–62
- 22 Fujisawa I. Magnetic resonance imaging of the hypothalamic-neurohypophyseal system. *J Neuroendocrinol* 2004;16:297–302
- 23 Schaller B, Kirsch E, Tolnay M, Mindermann T. Symptomatic granular cell tumor of the pituitary gland: case report and review of the literature. *Neurosurgery* 1998;42:166–170, discussion 170–171
- 24 Luse SA, Kernohan JW. Granular-cell tumors of the stalk and posterior lobe of the pituitary gland. *Cancer* 1955;8:616–622
- 25 Tomita T, Gates E. Pituitary adenomas and granular cell tumors. Incidence, cell type, and location of tumor in 100 pituitary glands at autopsy. *Am J Clin Pathol* 1999;111:817–825
- 26 Mumert ML, Walsh MT, Chin SS, Couldwell WT. Cystic granular cell tumor mimicking Rathke cleft cyst. *J Neurosurg* 2011;114: 325–328
- 27 Buschmann U, Gers B, Hildebrandt G. Pilocytic astrocytomas with leptomeningeal dissemination: biological behavior, clinical course, and therapeutical options. *Childs Nerv Syst* 2003;19: 298–304
- 28 Fleischman A, Brue C, Poussaint TY, et al. Diencephalic syndrome: a cause of failure to thrive and a model of partial growth hormone resistance. *Pediatrics* 2005;115:e742–e748
- 29 Coakley KJ, Huston J III, Scheithauer BW, Forbes G, Kelly PJ. Pilocytic astrocytomas: well-demarcated magnetic resonance appearance despite frequent infiltration histologically. *Mayo Clin Proc* 1995;70:747–751
- 30 Arslanoglu A, Cirak B, Horska A, et al. MR imaging characteristics of pilomyxoid astrocytomas. *AJNR Am J Neuroradiol* 2003;24: 1906–1908
- 31 Kayama T, Tominaga T, Yoshimoto T. Management of pilocytic astrocytoma. *Neurosurg Rev* 1996;19:217–220
- 32 Sutton LN, Molloy PT, Sernyak H, et al. Long-term outcome of hypothalamic/chiasmatic astrocytomas in children treated with conservative surgery. *J Neurosurg* 1995;83:583–589
- 33 Pollack IF, Hurtt M, Pang D, Albright AL. Dissemination of low grade intracranial astrocytomas in children. *Cancer* 1994;73: 2869–2878