Spindle cell oncocytoma of the pituitary gland

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OBJECTIVE The authors report the diagnosis, management, and outcomes of 6 cases of spindle cell oncocytoma (SCO) in an effort to guide clinical diagnosis and management of these uncommon lesions.

METHODS This study is a retrospective review of cases involving adult patients who underwent resection of pituitary lesions at the authors' institutions between January 2000 and October 2017. The authors identified patients with histopathological confirmation of SCO and collected clinical data, including preoperative, perioperative, and postoperative management, complications, and outcomes.

RESULTS Six patients with SCO were identified. Clinical findings at initial presentation included visual disturbances, dizziness, and headache. All patients underwent resection. Four resections were initially performed by the transsphenoidal approach, and 2 resections were performed by craniotomy at an outside institution with subsequent transsphenoidal reoperations. Neither necrosis nor increased mitotic activity was seen in the tumor samples. All samples stained positive for S100 protein and thyroid transcription factor 1 and negative for glial fibrillary acidic protein and pituitary hormones. Five of the samples stained positive for epithelial membrane antigen. The average MIB-1 index was 8.3% (range 2–17). Postoperatively, 3 of the 6 patients received further treatment for progression of residual tumor or for recurrence, 2 have stable residual tumor, and 1 has had no recurrence after gross-total resection. Two patients developed postoperative complications of transient sixth cranial nerve palsy and diplopia. There were no other complications.

CONCLUSIONS SCO poses both a diagnostic and therapeutic challenge. These tumors are often initially misdiagnosed as nonfunctional pituitary adenomas because of their sellar location and nonspecific symptomatology. Postoperatively, SCO must also be distinguished from other neoplasms of the posterior pituitary gland through histopathological examination. Resection of SCO can be challenging, given its highly vascular and adherent nature. Long-term follow-up is critical, as the tumor is associated with higher recurrence and progression rates compared to other benign neoplasms of the sella.

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KEYWORDS spindle cell oncocytoma; neurosurgery; transsphenoidal; pituitary surgery

SPINDLE cell oncocytomas (SCOs) are non-neuroendocrine neoplasms of the pituitary gland. Spindle cell oncocytoma was first included in the World Health Organization (WHO) classification of central nervous system (CNS) tumors in 2007 after the tumor was described in 2002.^{12,18,29} Roncaroli et al. defined SCO as spindled in appearance, with eosinophilic cytoplasm and numerous

swollen mitochondria, immunoreactivity for vimentin, epithelial membrane antigen (EMA), galectin-3, and S100, no expression of pituitary hormones, and a benign histopathology due to lack of invasiveness and low proliferative activity.²⁹

Clinically, SCOs are extremely rare. In a 7-year series of transsphenoidal (TS) operations at a single tertiary care

ABBREVIATIONS CN = cranial nerve; CNS = central nervous system; EMA = epithelial membrane antigen; GFAP = glial fibrillary acidic protein; GTR = gross-total resection; OSH = outside hospital; SCO = spindle cell oncocytoma; S100 = S100 protein; TS = transsphenoidal; TTF-1 = thyroid transcription factor 1; WHO = World Health Organization.

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TABLE 1. Presenting characteristics of the 6 SCO cases treated at our institutions

Case No.	Age (yrs), Sex	Presenting Sx	Primary, Recurrence, or Progression	Size (cm)	Tx	Intraop Events	Outcome/Subsequent Tx
1*	66, F	Dizziness, nausea, diaphoresis	Primary	1.7 × 2.1 × 2.4 (inf); 1.5 × 1.0 × 1.3 (sup)	TSR		Mild CN VI palsy resolved w/ dexameth; stable residual tumor (100 mos)
2*	50, M	Dizziness	Primary	1.2 × 1.4 × 1.3	TSR	Signif intraop venous bleeding	Stable residual tumor (30 mos)
3*	63, M	VD	Progression (3 mos postop from craniotomy at OSH)	2.7 × 2.7 × 1.9	TSR		Repeat TSR for tumor progression (3 mos postop); craniotomy for tumor progression (42 mos after repeat TSR)
4	59, F	HA, thyroid & adrenal hypopit, VD	Primary (transferred from an OSH due to intraop bleeding during craniotomy)		TSR	Excessive intraop bleeding	Recurrence 6 yrs after GTR, treated w/ repeat TSR, GKRS; stable (79 mos after initial presentation)
5	77, M	VD	Primary	2.4 × 2.8 × 2.2	TSR		Stable after GTR (12 mos)
6	56, F	Eye ball heaviness, nausea, dizziness	Progression (8.5 yrs after 2 TSRs, 1 craniotomy, CKRS at OSH)	3.8 × 4.2 × 4.1	TSR		Diplopia resolved 1 mo postop; proton beam therapy for residual tumor; stable residual tumor (38 mos after initial op at our institution)

CKRS = CyberKnife radiosurgery; CN = cranial nerve; dexameth = dexamethasone; GKRS = Gamma Knife radiosurgery; HA = headache; hypopit = hypopituitarism; inf = inferior; OSH = outside hospital; signif = significant; sup = superior; Sx = symptoms; TSR = transsphenoidal resection; Tx = treatment; VD = visual deficit.

* These cases were previously reported with limited clinical detail in a study of SCO exome profiles.²³

center, SCO accounted for 0.51% of final pathological diagnoses among nearly 800 transnasal, TS operations.⁶ In reviewing the literature from 2002 to 2018, approximately 40 cases of SCO have been reported. Because of their similarity on imaging to other pituitary neoplasms and nonfunctional hormonal status, SCOs are frequently misdiagnosed preoperatively, often as nonfunctional pituitary adenomas.²⁶ Historically, there has been much debate about the origin of and intersection among SCO, pituitary adenoma, and granular cell tumors, all of which share similar histopathological features.^{7,16,22,36} In the fourth edition of the WHO classification of tumors of the endocrine glands, pituitary SCO—along with pituitary adenoma, granular cell tumor of the sella, and sellar ependymoma—was classified as a tumor of the posterior pituitary.¹⁷ Previously, SCOs were thought to arise from the adenohypophysis.²⁹ There is support for the idea that these tumors, which remain classified as distinct tumor subtypes, may be variations of the same pathophysiology and may arise from a common progenitor cell in the posterior pituitary, the pituicyte.^{17,21}

We describe the presentation, management, pathological characteristics, and outcomes of 6 cases with long-term follow-up. In doing so, we aim to advance the clinical understanding of these lesions, as their diagnosis and management is often difficult and complex.

Methods

We retrospectively reviewed cases in which patients underwent resection of pituitary lesions performed by the senior authors at 2 large academic centers between January 2000 and October 2017. We identified patients who had histopathological confirmation of SCO. Three of the

cases included have been previously published in a study on the molecular etiology of SCO.²³ In the present study, we add additional neurosurgical context and long-term follow-up information for these cases. The formal histological diagnosis was characterized by spindled cellular appearance with eosinophilic cytoplasm and immunoreactivity for glial fibrillary acidic protein (GFAP), S100, thyroid transcription factor 1 (TTF-1), EMA, and pituitary hormones. We collected clinical data, including preoperative, perioperative, and postoperative management, complications, and outcomes.

Results

Six patients were diagnosed with SCO over a 17-year period (Table 1). Of the 6 patients, 3 were women and 3 were men; the patients' mean age was 62 years (range 50–77 years).

Three patients (cases 1, 2, and 5) presented to our institutions with newly diagnosed sellar masses and recent-onset symptoms that included dizziness, nausea, and diaphoresis (case 1); dizziness (case 2); and visual disturbances, including temporal field loss and afferent pupillary defects (case 5). All 3 patients underwent TS operations. Gross-total resection (GTR) was achieved in case 5, with no evidence of residual or recurrent tumor at 12 months postoperatively. The patients in cases 1 and 2 both had residual tumor on postoperative MRI that has been stable at 100 and 30 months postoperatively, respectively (Fig. 1A, B, D, and E). Intraoperatively, significant venous bleeding was noted in case 2, but no postoperative deficits were present. The patient in case 1 developed cranial nerve (CN) VI palsy, which resolved with a 10-day course

FIG. 1. Preoperative and postoperative coronal contrast-enhanced T1-weighted MR images. **A:** Preoperative image showing a dumbbell-shaped intrasellar and suprasellar SCO (case 1). **B:** Preoperative image showing an intrasellar tumor that was initially misdiagnosed as a pituitary adenoma (case 2). **C:** Preoperative image of a SCO obtained after a craniotomy at an OSH (case 3). **D:** Follow-up image obtained 100 months postoperatively showing stable residual tumor (case 1). **E:** Follow-up image obtained 30 months postoperatively showing stable residual tumor (case 2). **F:** Postoperative MR image showing residual after 2 transsphenoidal resections and 2 craniotomies (case 3).

of dexamethasone. There were no other surgical complications in these 3 cases. The presenting symptoms of all 3 patients improved with surgery.

The other 3 patients (cases 3, 4, and 6) had prior resection of tumor involving the pituitary region at outside hospitals (OSHs) before presentation. All patients eventually underwent TS resection at one of the 2 centers included in this study. The patient in case 3 presented to our institution 3 months after undergoing craniotomy at an OSH for tumor progression. He initially presented to the OSH and to our institution with visual disturbance. The patient underwent 2 subtotal TS resections and a craniotomy for tumor progression 3 months, 6 months, and 4 years after initial resection at the OSH (Fig. 1C and F). Because of the craniotomy was performed only recently, no follow-up information is available. The patient's vision did not improve. The patient in case 4 was transferred to our institution after an aborted craniotomy due to excessive hemorrhage during the operation. A TS operation was performed with no evidence of residual tumor on postoperative MRI. The

FIG. 2. Photomicrograph of SCO (case 1). H & E; original magnification $\times 600$. Figure is available in color online only.

patient's visual disturbances, cranial nerve palsy, diplopia, and headache improved after TS resection. Six years later, the tumor recurred, with symptoms of left sided cranio-orbital pain and left CN VI palsy. The patient underwent repeat TS resection and Gamma Knife radiosurgery. The residual tumor is currently stable 79 months after initial presentation; she has persistent left-sided headache but her diplopia and left CN VI palsy have both resolved. The patient in case 6 presented to our institution 9 years after undergoing 2 TS resections, one craniotomy, and CyberKnife therapy at an OSH. She presented with eyeball heaviness, nausea, and dizziness. She underwent TS resection and received proton beam therapy for enlarging residual tumor. The patient developed diplopia that resolved 1 month after the operation, and the residual tumor is currently stable 38 months postoperatively.

On pathological examination, SCO was diagnosed by spindled cellular appearance with abundant granular eosinophilic cytoplasm (Fig. 2) in all 6 cases. All samples stained positive for S100 and TTF-1 (Fig. 3) and negative for GFAP and pituitary hormones (Table 2). Five of the 6 samples stained positive for EMA. No necrosis or increased mitotic activity was seen in any of the cases. The mean MIB-1 index was 8.3% (median 5.5, range 2–17).

Discussion

SCO is a rare and often misdiagnosed neoplasm of the posterior pituitary. SCOs generally arise in the region of the sella and present similarly to nonfunctional pituitary adenomas, making it difficult to distinguish them from other common pituitary lesions based on imaging alone.^{24,26} Preoperative symptoms are not diagnostic, as common symptoms of SCO, including visual disturbances, headache, and hypopituitarism, are nonspecific results of mass effect on parasellar structures. SCOs have no immunoreactivity for pituitary hormones, nor neuroendocrine markers such as chromogranin and synaptophysin.^{22,29} The tumors have a distinctive microscopic appearance, however, with spindled cells containing granular eosinophilic cytoplasm, and a distinct immunohistochemical

FIG. 3. Photomicrograph of SCO, stained by immunohistochemistry for TTF-1 (NKX2-1). Original magnification $\times 400$ (case 2). Figure is available in color online only.

profile that distinguishes them from adenomas on pathological examination.

In this paper, we present 6 cases of SCO treated at 2 multidisciplinary pituitary centers in an effort to discuss contemporary management of these complex lesions. Prior to this study, the largest series of SCOs in the literature was reported in the seminal paper of Roncaroli et al. in 2002, which included 5 patients, and defined the novel neoplasm “spindle cell oncocytoma.”²⁹ In 2007, the WHO included SCO in the classification of CNS tumors as a distinct non-neuroendocrine lesion.

Not including the cases reported in this paper (or the subset reported earlier by Miller et al.²³), a total of 39 cases of SCO have been reported in the literature as case reports and case series (Table 3).^{1–5,8–11,13–15,19,20,23–36} These lesions are often initially managed by a TS approach because preoperative radiological features are suggestive of a pituitary adenoma.²⁶ Of 37 cases for which type of resective surgery was reported in the literature, 32 (86.5%) were managed initially with TS resection and 5 (13.5%) were managed initially with craniotomy. In the current case series, the senior authors performed TS resection on all 6 patients. However, 3 patients had undergone prior craniotomy.

SCO has a significant risk of progression or recurrence. Because of the vascular and adherent nature of the tumor, subtotal resection of SCO is common. Gross-total resection (GTR) was achieved in only 2 of the cases presented here, and in one of those 2 cases, the tumor subsequently recurred. Of the 41 cases with follow-up information, including our own, 39% were recurrent at the time of surgery, recurred postoperatively after GTR, or required additional surgery for residual tumor. The progression and recurrence rate of this tumor may be higher than reported given variable follow-up durations. There are 8 reports in the literature of individuals receiving radiation after resection.

These high rates of recurrence, reoperation, and adjuvant radiation suggest a more clinically aggressive course for SCO compared to other lesions of the sellar region. The 6 cases reported here also fit this pattern: only 3 were

managed successfully with a single TS operation (mean follow-up 47 months). The remaining 3 lesions required the following additional interventions: a prior craniotomy at an OSH, a reoperation by the TS approach (the same year the patient presented), and a craniotomy for recurrence; a TS reoperation followed by Gamma Knife radiosurgery; and 2 TS operations, reoperation by craniotomy, and CyberKnife at an OSH prior to resection and proton beam radiotherapy after resection at our institution.

In a summary of the 2017 WHO classification of tumors of endocrine glands, Lopes reviewed the features of tumors of the posterior pituitary, including granular cell tumor, SCO, pituicytoma, and sellar ependymoma.¹⁷ These tumors remain classified as distinct tumor entities in the new classification scheme. It is believed, however, that the tumors may be subtypes that arise from a common progenitor cell of the posterior pituitary, the pituicyte, and are variations of the same pathophysiology (Table 4). Strong staining for EMA would support a histological diagnosis of SCO. In our series, the tumors were EMA-positive in 5 of 6 cases. The SCO in case 3 was initially EMA-negative but had focal EMA positivity on subsequent resection and pathological analysis.²³ Equivocal or negative EMA staining could indicate that this tumor is another variation of a pituitary gland tumor or that the sample was not representative of the tumor’s true characteristics. As seen in the literature review of immunohistochemical markers, including in our own samples, SCO is generally reactive for S100 (93% of samples tested), EMA (95%), and TTF-1 (100%), and only rarely reactive for GFAP (10.8%) (Table 2). Although Roncaroli et al. noted the benign nature of SCO with a low proliferative index, we have demonstrated this is not exclusively the case. Along with the high rates of recurrence and progression of the tumor, it is demonstrated in the literature review and in our own cases that SCO can have a high proliferative index measured by MIB-1/Ki-67 index. In 2 of our cases, the MIB-1 index was above 10%.

Of note, SCOs are highly vascular tumors that can cause significant intraoperative bleeding.¹⁷ Borges et al. report a case of recurrent subclinical intratumoral bleeding occurring in a recurrent SCO.³ In a review of the literature within this paper, Borges found that 29% of 28 case reports reviewed noted excessive intraoperative bleeding and 46% of cases noted the tumor to be highly vascular intraoperatively. There were also 3 cases of spontaneous tumor hemorrhage. In the cases that we present in the present study, 2 patients were noted to have more than a normal amount of intraoperative bleeding, and one of the two was transferred from an OSH after excessive intraoperative bleeding during the initial resection. Careful attention must be paid to the potential for significant intraoperative bleeding when dealing with a tumor of the posterior pituitary gland, especially SCO.

On molecular analysis, recent reports have identified novel mutations in SCO tumors, including co-occurring somatic *HRAS*-activating mutations and *MEN1* frameshift mutations, which may contribute to their clinical aggressiveness.²³ As a result of the particularly aggressive nature of these lesions, patients who harbor SCO should receive frequent postoperative radiographic and clinical monitor-

TABLE 2. Pathological characteristics of SCO cases reported in the literature

Authors & Year	Necrosis	Mitosis	MIB-1/Ki-67 Index (%)	EMA	TTF-1	S100	GFAP
Roncaroli et al., 2002	Absent	Absent	1	+	NA	+	–
	Absent	Absent	3	+	NA	+	–
	Focal	Rare	1	+	NA	–	–
	Absent	Absent	3	+ (rare)	NA	+	–
	Absent	Rare	5	+	NA	+	–
Kloub et al., 2005	Absent	Absent	18	+	NA	+	–
	Focal	Increased	20	+	NA	+	–
Dahiya et al., 2005	Absent	Absent	1	+	NA	+	–
	Absent	Absent	8	+	NA	+	–
Vajtai et al., 2006	Absent	Absent	<1	+	NA	+	+ (few)
Coiré et al., 2009	NA	NA	NA	NA	NA	NA	NA
Borota et al., 2009	NA	NA	NA	+	NA	+	NA
Matyja et al., 2010	Absent	Rare	5	+	NA	+	–
	Absent	Rare	1	+	NA	+	–
Demssie et al., 2011	Absent	Absent	<1	+	NA	+	NA
Vajtai et al., 2011	Absent	Absent	1.5–2	+	+	+	–
Mlika et al., 2011	Absent	Low	NA	+	+	+	–
Romero-Rojas et al., 2011	NA	Low	2	+	NA	+	–
Borges et al., 2011	Absent	Low	3.2	+ (rare)	NA	+	–
Ogiwara et al., 2011	Absent	Rare	5	+	+	+	NA
Singh et al., 2012	Absent	Absent	<1	+	NA	+	–
Alexandrescu et al., 2012	Absent	Absent	<5	+	NA	+	–
Fujisawa et al., 2012	Absent	Absent	3	+	NA	+	–
Rotman et al., 2014	NA	Absent	2.5	+	NA	–	–
Mu et al., 2015	NA	Absent	3	+	+	+	–
	NA	Absent	1.5	+	+	+	–
Zygourakis et al., 2015	NA	NA	<5	+	+	–	–
	NA	NA	NA	+	+	+	+
Custodio et al., 2016	NA	NA	3	+	+	+	–
Hasiloglu et al., 2016	Absent	Absent	NA	+	NA	+	NA
	Absent	Absent	NA	+	NA	+	NA
	Absent	Absent	NA	+	NA	+	NA
Vuong et al., 2016	Absent	Absent	<1	+	+	+	NA
Guadagno et al., 2016	Absent	Absent	11	+	+	+	–
Billeci et al., 2017	Absent	Absent	2	NA	+	+	–
	Absent	Low	8	NA	+	+	–
Osman & Wild, 2017	Absent	Absent	Low	+	+	+	+
Manoranjan et al., 2017	Absent	Absent	2–4	–	+	+	+
Sali et al., 2017	Absent	Absent	6–8	+	+	+	–
Current study, case 1*	Absent	Absent	5	+	+	+	–
Case 2*	Absent	Absent	2	+	+	+	–
Case 3*	Absent	Absent	5	–	+	+	–
Case 4	Absent	Absent	15	+	+	+	–
Case 5	Absent	Absent	6	+	+	+	–
Case 6	Absent	Absent	17	+	+	+	–

EMA = epithelial membrane antigen; GFAP = glial fibrillary acidic protein; NA = data not available; S100 = calcium binding S100 protein; TTF-1 = thyroid transcription factor 1.

* Also previously reported by Miller et al.²³

TABLE 3. Literature review of SCO cases

Authors & Year	Age (yrs), Sex	Presenting Sx	Primary or Progression/Recurrence	Size (cm)	Tx	Outcome/Subsequent Tx
Roncaroli et al., 2002	53–71 (mean 61.6); 2F, 3M	PHP	Primary	NA	TSR	FU 2–68 mos (mean 35.4 mos); no recurrences noted
		PHP	Primary	NA	TSR	
		PHP	Primary	NA	TSR	
		PHP, VD	Primary	NA	TSR	
		PHP, VD	Primary	NA	Craniotomy	
Kloub et al., 2005	71, F	VD, PHP (mild)	P/R: primary TSR 11 yrs prior; 1st sign of recurrence 8 yrs prior	NA	TSR	Add'l resection for residual tumor 1 yr postop
	76, M	Epistaxis	P/R: primary TSR 10 yrs prior w/ add'l resection & radiation 7 yrs prior	NA	TSR	NA
Dahiya et al., 2005	26, M	HA, VD, N/V, impotence	Primary	1.5–2 (diam)	TSR, craniotomy, proton beam radiation	Stable (7 yrs)
	55, F	HA, VD	Primary	6.5 × 3.3 × 4.0	TSR	Stable (6 mos)
Vajtai et al., 2006	48, F	Fatigue, VD	Primary	1.8 × 1.5 × 1.3	TSR	Stable (16 yrs)
Coiré et al., 2009	NA	NA	Primary	NA	TSR	Add'l TSR & radiation 5 mos postop
Borota et al., 2009	NA	NA	NA	NA	TSR, RT	Regrowth over 30-mo FU period
Matyja et al., 2010	63, F	PHP, N/V, HA, VD	Primary	2.1 × 1.8 × 1.9	TSR	Stable (28 mos)
	65, F	PHP	P/R: primary TSR 3 yrs prior	1.8 × 1.9 × 2.1	Frontal craniotomy	Stable (20 mos)
Demssie et al., 2011	59, M	PHP, VD, N/V	Primary	NA	TSR, RT	2 add'l TSR 9 mos postop
Vajtai et al., 2011	55, F	PHP	Primary	2.7 × 2.6 × 2.5	TSR	
Mlika et al., 2011	45, F	VD, HA	Primary	2.0 × 1.5 × 1.0	TSR	Stable (3 mos)
Romero-Rojas et al., 2011	42, F	Oligomenorrhea	Primary	3.2 × 3.2 × 3.4	"Resection"	NA
Borges et al., 2011	70, F	VD	Primary	3.3 × 2.4 × 3.0	TSR	Recurrence & add'l TSR 13 yrs postop
Ogiwara et al., 2011	39, M	HA, memory loss	P/R: primary craniotomy & radiation 13 mos prior; add'l resection 4 mos prior w/ residual	2.7 × 2.4 × 2.8	TSR	Stable residual (1 yr)
Singh et al., 2012	68, M	VD, HA	Primary	3.1 × 2.9 × 3.0	TSR	Died from unrelated causes 1 mo postop
Alexandrescu et al., 2012	24, F	HA, amenorrhea, VD	Primary	2.5 × 1.8	TSR	Stable (6 mos)
Fujisawa et al., 2012	68, M	PHP, VD	Primary	NA	TSR	Transcranial re-resection for residual tumor & radiation 18 mos postop
Rotman et al., 2014	88, M	PHP, VD, fatigue	Primary	2.7 × 2.0 × 1.7	TSR	NA
Mu et al., 2015	35, F	Amenorrhea, lactation, VD	Primary	2.5 × 3.0 × 1.0	Craniotomy	Stable (21 mos)
	62, F	Incidental finding	Primary	2.3 × 1.7 × 2.0	Craniotomy	Stable (15 mos)
Zygourakis et al., 2015	31, F	VD, HA	Primary	2.2 (diam)	TSR	Stable (6 mos)
	53, F	HA	Primary	0.7 (diam)	Biopsy	Stable (2 mos)
Custodio et al., 2016	60, M	N/V, syncope, PHP, hyponatremia	Primary	3.1 × 2.3 × 2.0	TSR	Stable (18 mos)

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TABLE 3. Literature review of SCO cases

Authors & Year	Age (yrs), Sex	Presenting Sx	Primary or Progression/Recurrence	Size (cm)	Tx	Outcome/Subsequent Tx
Hasiloglu et al., 2016	40, M	PHP	Primary	2.1 × 1.9 × 3.6	TSR	Add'l TSR 1 yr postop for residual tumor
	60, M	HA, VD	Primary	3.1 × 2.0 × 2.3	TSR	Stable (12 mos)
	55, M	HA, VD	Primary	2.0 × 1.9 × 1.8	TSR	Stable (6 mos)
Vuong et al., 2016	70, M	HA, VD	Primary	6.0 × 5.5 × 4.5	TSR	Stable (6 mos)
Guadagno et al., 2016	77, M	HA, VD	Primary		TSR	Stable (14 mos)
Billeci et al., 2017	61, M	HA	Primary	2.2 × 1.8 × 2.7	TSR	Add'l TSR for residual tumor 16 mos postop; stable (14 mos)
	65, F	HA, VD	Primary	2.0 × 1.5 × 1.0	TSR	Stable (28 mos)
Osman & Wild, 2017	56, M	HA, altered LOC, VD	Primary	2.5 × 4.4 × 2.5	Craniotomy (urgent), EVD	Stable (6 mos)
Manoranjan et al., 2017	60, M	VD	P/R: primary resection 13 yrs prior; biopsy & RT for residual tumor 11 yrs prior	2.6 × 3.0 × 2.4	TSR	Stable (9 mos)
Sali et al., 2017	64, M	VD	P/R: primary TSR 4 yrs prior	2.2 × 2.1 × 2.5	TSR	NA

Add'l = additional; diam = diameter; EVD = external ventricular drain; FU = follow-up; LOC = level of consciousness; N/V = nausea/vomiting; PHP = panhypopituitarism; P/R = progression/recurrence; RT = radiotherapy; TSR = transsphenoidal resection; VD = visual deficit.

The 6 cases reported in the current study (including the 3 previously reported by Miller et al.²³) are not included in this table. For a summary of those cases, please see Table 1.

ing. In most cases of sellar lesions, annual imaging is sufficient.

In cases of recurrent tumor or growth of residual tumor after subtotal resection, patients should seek multidisciplinary management, with consideration given to both reoperation and possible radiation therapy. In two of our cases (cases 4 and 6), progressive growth of residual tumor halted after adjuvant radiation.

There are also case reports of SCOs managed transcranially, which has been posited to be of benefit given their highly vascular and adherent nature.^{9,20,25,29} In this series, one operation at an OSH had to be aborted because of intraoperative bleeding during a standard craniotomy (case 4), and it is possible that the transcranial approach may provide more intraoperative maneuverability to deal with

excessive bleeding and better access to adherent areas of tumor. Nevertheless, each of the 6 SCOs reported on here was ultimately managed by the TS approach. With proper adjuvant therapy and careful monitoring, SCO can be successfully treated transsphenoidally, and even in cases of subtotal resection, patients can experience substantial benefit due to relief of mass effect on the pituitary gland and optic chiasm.

The limitations of our study include the retrospective nature, relatively small sample size related to the rareness of the entity, and heterogeneous management of the 6 cases presented. However, we believe that our study, which is the largest case study of SCO to date, offers value by discussing current diagnostic, therapeutic, and management strategies. In addition, we thoroughly review the literature with

TABLE 4. TTF-1–positive tumors of the posterior pituitary gland

Tumor Subtype	Histology & Ultrastructure (EM)	Immunoreactivity	Distinguishing Features
All		TTF-1 (strong nuclear immunoreactivity) ^{16,22} S100 (variable staining)	
SCO	Spindle or epithelioid cells in intertwining fascicles w/ granulated eosinophilic cytoplasm; abundant mitochondria by EM	EMA (strong) GFAP (rarely positive)	Increased tendency to bleed during the op
Pituitaryoma	Fibrillary cells arranged in fascicles w/ elongated nuclei; abundant intermediate filament processes by EM	EMA (variable) GFAP (positive generally)	
Granular cell tumor	Polygonal cells w/ central nuclei & PAS-positive, granular cytoplasm; abundant lysosomes by EM	EMA (variable) GFAP (rarely positive)	

EM = electron microscopy; PAS = periodic acid-Schiff.

a focus on the pathological characteristics of SCO in the context of the updated 2017 WHO classification of SCO.

Conclusions

SCO poses both a diagnostic and therapeutic challenge. Because of its sellar location and common presenting symptoms of visual disturbances, headache, and hypopituitarism, it is often misdiagnosed as a nonfunctional pituitary adenoma. Because of the highly vascular and adherent nature of these lesions, resection of SCO can be hazardous but even subtotal resection can interrupt progression and provide symptomatic relief. In addition, SCO is associated with a high recurrence and progression rate compared to other benign neoplasms of the sella, and vigilant long-term follow-up is recommended.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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Conception and design: Laws, Giantini Larsen, Cote, Zaidi, Smith, Jane. Acquisition of data: Giantini Larsen, Cote, Zaidi, Bi, Schmitt, Iorgulescu, Miller, Lopes, Jane. Analysis and interpretation of data: Giantini Larsen, Cote, Schmitt, Miller, Lopes. Drafting the article: Giantini Larsen, Cote, Schmitt. Critically revising the article: Laws, Giantini Larsen, Cote, Zaidi, Bi, Schmitt, Iorgulescu, Miller, Smith, Lopes. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Laws. Administrative/technical/material support: Laws. Study supervision: Laws, Smith, Jane.

Supplemental Information

Previous Presentations

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