

Case Report

Spindle cell oncocytoma of the pituitary and pituicytoma: Two tumors mimicking pituitary adenomaHideki Ogiwara, Steve Dubner¹, Stephen Shafizadeh, Jeffrey Raizer², James P. ChandlerDivisions of Neurosurgery, ¹Pathology, and ²Neurology, Northwestern University, Feinberg, School of Medicine, Chicago, Illinois, USE-mail: Hideki Ogiwara - hideki_o@d5.dion.ne.jp; Steve Dubner - sdubner305@yahoo.com; Stephen Shafizadeh - sshafizadeh@nmff.org; Jeffrey Raizer - jraizer@nmff.org;*James P. Chandler - jchandler@nmff.org

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Abstract

Background: Spindle cell oncocytoma (SCO) and pituicytoma are rare nonfunctioning tumors of the pituitary. Both tumors are low grade and macroscopically indistinguishable from a nonfunctioning pituitary adenoma. We report one case of SCO and one case of pituicytoma and review the previous literature.

Case Description: One patient was a 39-year-old man who presented with progressive headache, visual blurring, and polyuria of 3-year duration. He underwent partial resection (30% of the tumor) and postoperative adjuvant radiation therapy. Histopathology revealed SCO. However, after 9 months, the residual tumor grew and partial resection (70% of the tumor) was performed again. Four months after the second surgery, the tumor recurred again and he underwent transsphenoidal resection of the tumor with stable residual tumor to date. The other patient was a 59-year-old man who presented with a 3-month history of visual decline, fatigue, difficulty in writing, and polyuria. He underwent transsphenoidal resection (total) of the tumor. Histopathology revealed pituicytoma. He has been stable without evidence of recurrence for 1 year and 4 months.

Conclusion: To date, there are 15 reported cases of SCO and 45 reported cases of pituicytoma including our cases. An incomplete resection of the tumor was a significant risk factor for recurrence in both SCO and pituicytoma ($P = 0.0014$ and $P = 0.019$, respectively). These tumors have a tendency to be hypervascular, which may hamper total resection. Epithelial membrane antigen (EMA) and mitochondria positivity is characteristic to SCO and they are considered to be important immunomarkers to distinguish these tumors.

Key Words: Pituicytoma, recurrence, spindle cell oncocytoma, total resection

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Quick Response Code:**INTRODUCTION**

Spindle cell oncocytoma (SCO) of the pituitary and pituicytoma are rare nonfunctional tumors, which have recently been codified as distinct entities by the 2007 WHO classification of central nervous system (CNS)

tumors. SCO is defined as a spindled-to-epithelioid, oncocytic, nonendocrine neoplasm of the anterior hypophysis that manifests in adults and follows a benign clinical course.^[11,26] Pituicytoma is a rare, solid, low-grade, spindle cell, glial neoplasm of adults that was thought to originate in the neurohypophysis or

infundibulum.^[8] Recent reports suggested the origin of pituicytoma to be from folliculostellate cells of the anterior pituitary, which are supporting cells in the anterior pituitary gland of diverse function. Both SCO and pituicytoma might be derived from folliculostellate cells.^[5,27,33] Unlike pituitary adenomas, these tumors do not demonstrate immunoreactivity for neuroendocrine markers (chromogranin, synaptophysin) and pituitary hormones but coexpress vimentin and S-100 protein. Both tumors have a tendency to be hypervascular. SCOs are characterized by a mitochondrial accumulation by ultrastructural analysis.

To date, there are 14 reported cases of SCO^[2,3,7-9,18,27,34] and 44 reported cases of pituicytoma.^[1,4,6,10,12-17,19-24,28-33,35,36] We review those previously reported cases and present our recommendations for the management of these rare tumors.

MATERIALS AND METHODS

Surgical specimens were formalin fixed and routinely processed. Five-micron-thick tissue sections were stained by hematoxylin and eosin, and immunohistochemistry. The following antibodies were applied: anti-gliofibrillary acidic protein (GFAP; polyclonal, 1:2800; DAKO), anti-S-100 protein (polyclonal, 1:2000; DAKO), antithyroid transcription factor 1 (TTF-1; monoclonal, prediluted; Cell Marque), anti-EMA (epithelial membrane antigen; monoclonal, 1:500; DAKO), anti-calretinin (monoclonal, prediluted; Ventana), anti-Ki-67 (MIB-1; monoclonal, 1:200; DAKO), anti-galectin-3 (monoclonal, 1:25; Invitrogen), anti-CD34 (monoclonal, 1:25; DAKO), anti-CD57 (monoclonal, 1:50; Becton Dickenson), anti-CD68 (monoclonal, 1:400; DAKO), anti-mitochondria (monoclonal, 1:200, Leinco Technologies), anti-chromogranin (monoclonal, prediluted; Ventana), and anti-synaptophysin (polyclonal, 1:50; DAKO).

CASE REPORT

Case 1 (spindle cell oncocytoma)

A 39-year-old man presented with progressive headache, loss of stamina and libido, visual blurring, and polyuria of 3-year duration to an outside hospital. Visual field assessment revealed a bitemporal hemianopia. Endocrinologic evaluation revealed low testosterone and high prolactin levels. He was started on bromocriptine and testosterone replacement. The MRI scan revealed a suprasellar lesion with the compression of the optic nerves [Figure 1a and b]. The patient underwent a transcranial partial resection (30%) of the tumor and subsequent radiation for the residual tumor. The total dose of radiation was 5040 cGy. The patient had a recurrence 9 months after the first surgery and underwent the second surgery (70% of the tumor resected). The patient

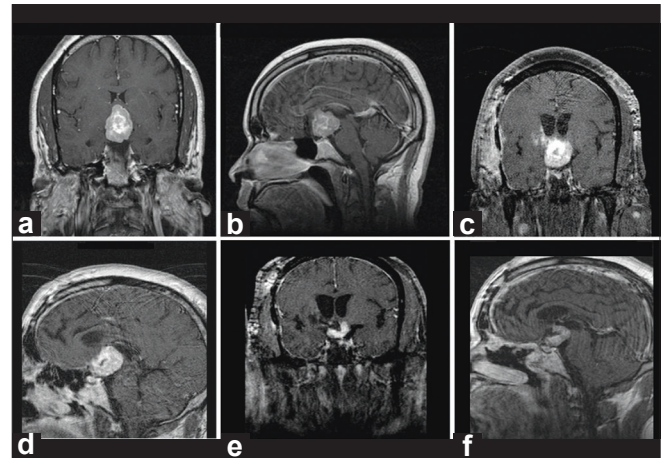


Figure 1: (a and b) Magnetic resonance images of the T1-weighted image with contrast demonstrated enhancing suprasellar mass. (c and d) Recurrent tumor. (e and f) Postoperative magnetic resonance images showed debulked tumor

presented to our clinic 4 months after the second surgery with worsening headache and memory loss. The serum sodium level was 140 mEq/l. The MRI showed a 2.7 × 2.4 × 2.8 cm enhancing suprasellar mass compressing the optic nerve ventrally without hydrocephalus, which had increased in size compared to the postoperative scan [Figure 1c and d]. Transsphenoidal resection was undertaken. The grayish gelatinous tumor was debulked and the optic chiasma was completely decompressed. The tumor was found to be firm and highly vascular. Due to the marked adherence of the capsule to neurovascular structures, a subcapsular decompression was the best that could be achieved. A histological examination revealed interlacing fascicles of spindled to epithelioid cells with eosinophilic and variably oncocytic cytoplasm. Mild to moderate nuclear atypia was present. Mitotic figures were rare [Figure 2a]. The MIB-1 labeling index was around 5%. The immunostain showed positivity for TTF-1, EMA, mitochondria [Figure 2b-d], S-100, and galectin-3, and was negative for CD34 and CD68. A diagnosis of SCO was made based on location, histology, and its characteristic staining properties, which was the same diagnosis as the initial one made at the previous institution. Visual acuity improved postoperatively and a significant reduction in the tumor bulk was seen on the postoperative MRI scan [Figure 1e and f]. The patient was stable with no evidence of recurrence at 1-year follow-up since the last surgery.

Case 2 (pituicytoma)

A 59-year-old man presented with a 3-month history of visual decline, fatigue, difficulty in writing, and polyuria. Visual field assessment revealed bitemporal hemianopia. The serum pituitary hormonal profile was grossly normal. The serum sodium level was 136 mEq/l. An MRI scan revealed a giant suprasellar clival lesion with the distortion

of the chiasm and invasion of the clivus [Figure 3a and b]. Transsphenoidal resection was undertaken. The tumor was gelatinous and hypervascular. The tumor was resected completely by alternating central debulking and mobilization of the capsule off the optic chiasm median eminence, hypothalamus, internal carotid artery branches including the superior hypophyseal, and the basilar quadrification. A histological examination revealed a solid neoplasm composed of elongate, bipolar spindle cells arranged in interlacing fascicles or in a storiform pattern. Individual tumor cells contained abundant eosinophilic cytoplasm and cell shapes ranged from short and plump to elongate and angulated. There was no significant cytoplasmic granularity or vacuolization. Mitotic figures

were rare [Figure 4a]. The MIB-1 labeling index was around 5%. The immunostain showed positivity for S-100 [Figure 4b], TTF-1, vimentin, and galectin-3. The tumor was non-immunoreactive for chromogranin, synaptophysin, EMA, GFAP, CD34, CD57, and CD68, and only focally positive for mitochondria. Given the histology, location, and immunostaining pattern, the most likely pathologic diagnosis was pituicytoma [Figure 4]. Visual acuity improved postoperatively and a postoperative MRI scan revealed no residual tumor [Figure 3c and d]. At the patient's 16-month follow-up examination, he was doing well and there was no evidence of tumor on imaging.

DISCUSSION

SCO was first described by Roncaroli *et al.* as a tumor containing fascicles of spindle cells with eosinophilic, granular cytoplasm, and a distinct immunophenotype which includes positive immunoreaction to vimentin, EMA, S-100, and galectin-3 with negative immunoreactions to pituitary hormones, synaptophysin, chromogranin, and cytokeratins. They suggested a benign nature based on the absence of cellular anaplasia, mitoses, and necrosis along with a low Ki-67 proliferation labeling index, and that no recurrence was observed in all five cases of their series with a mean follow-up of 3 years.^[27]

However, more recently a further nine additional cases have been described, six of which recurred.^[2,3,7-9,18,34] Two recurrent cases described by Kloub *et al.* demonstrated a high Ki-67 labeling index and one of these had mitosis

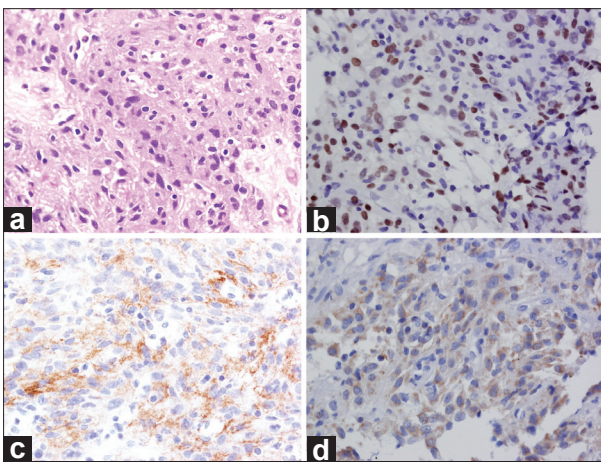


Figure 2: Histopathologic findings for patient 1 (original magnification, ×400). These images are from the patient's third resection. Microscopic evaluation reveals interlacing fascicles of spindled to epithelioid cells with eosinophilic, variably oncocytic cytoplasm. Mild to moderate nuclear atypia is present. (a) Mitotic figures are rare. Immunostains for (b) transcription factor 1, (c) epithelial membrane antigen, (d) and mitochondria are positive

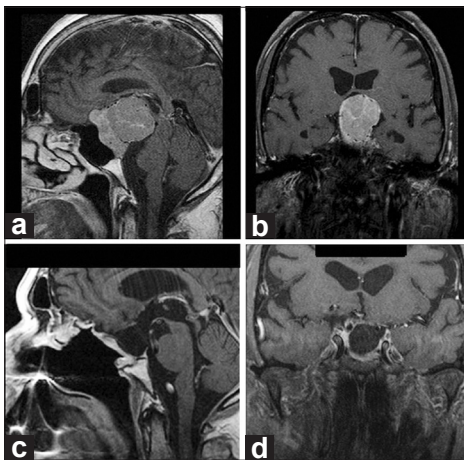


Figure 3: (a and b) Magnetic resonance images of the T1-weighted image with contrast demonstrated enhancing suprasellar mass. (c and d) Postoperative magnetic resonance images showed no residual tumor

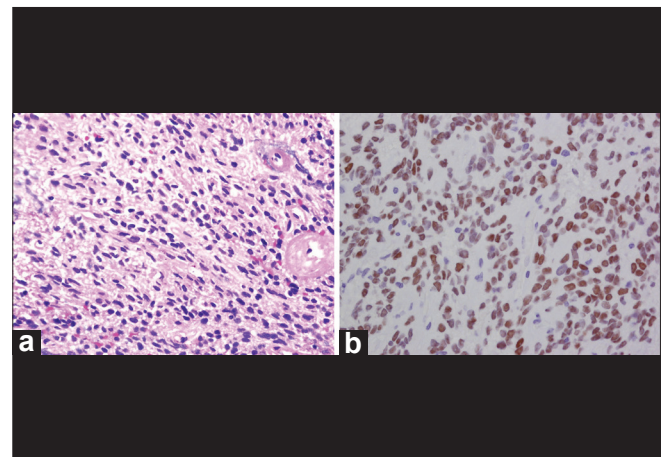


Figure 4: Histopathologic findings for patient 2 (original magnification of both, ×400). Microscopic examination reveals a solid neoplasm composed of elongate, bipolar spindle cells arranged in interlacing fascicles or in a storiform pattern. Individual tumor cells contain abundant eosinophilic cytoplasm and cell shapes range from short and plump to elongate and angulated. There is no significant cytoplasmic granularity or vacuolization. (a) Mitotic figures are rare. (b) Immunostain for transcription factor 1 is positive

and necrosis. Four cases demonstrated a low Ki-67 labeling index and showed no mitosis or necrosis. Our case also recurred 9 months after the partial resection, which showed a low Ki-67 labeling index (5%) without mitosis or necrosis. The mean time between the surgery and recurrence of seven cases including our case was 3.3 years (ranging from 5 months to 13 years). Six out of 7 (85.7%) recurrent cases underwent an incomplete resection at the original surgery. The incomplete resection of the tumor was a significant risk factor for recurrence ($P = 0.0014$; Figure 5). Seven out of 8 cases with a total resection did not recur (mean follow-up, 5.1 years).

The previous report described SCOs as firm, fibrous, and adherent to surrounding structures making dissection difficult especially in recurrent cases.^[8,9,18] These tumors have also been described as highly vascular.^[8,9] These characteristics were also observed in our case, and when present, can negatively impact the ability to carry out a complete resection.

Pituicytoma is a rare, solid, glial, and low-grade tumor of adult pituitary. Histologically, pituicytoma consists of elongate, bipolar spindle cells arranged in interlacing fascicles or assuming a storiform pattern.^[4,33] Mitotic figures are absent or rare. Immunohistologically, they show positivity for vimentin, S-100 protein and, to a variable degree, GFAP. In contrast to spindle cell oncocytoma, EMA is usually negative. Due to their slow growth and the possibility of curative surgery, pituicytomas correspond to WHO grade I.^[11]

Of 29 cases of pituicytoma with a detailed follow-up, 6 cases (20.7%) recurred. The Ki-67 labeling index was low and mitosis or necrosis was not observed in any recurrent case. The mean time between the original surgery and recurrence was 1.1 years (ranging from 5 months to 2 years). All the recurrent cases underwent an incomplete

resection at the original surgery. Similar to SCO, an incomplete resection of the tumor was a significant risk factor for recurrence ($P = 0.019$; Figure 6). Six out of 16 cases (37.5%) with an incomplete resection recurred. All 13 cases with a total resection did not have recurrence (mean follow-up, 2.0 years).

Pituicytomas have also been described as highly vascular like SCOs,^[1,12,13,17,19,24,31,33,35,36] which also applied in our pituicytoma case, and when present, may preclude complete resection.

The immunostain by S-100 was positive in all the reported cases of SCOs and pituicytomas. GFAP positivity varied in pituicytomas. The immunostain by GFAP was available in 38 cases of pituicytoma, of which 9 cases (23.7%) were negative for GFAP. The immunostain by galectin-3 was positive in our cases of SCO and pituicytoma. Rodríguez *et al.* showed that galectin-3 is expressed not only in SCO but also in pituicytoma and granular cell tumors. And they suggested that this marker is of little use to differentiate those diagnoses.^[25] Lee *et al.* recently reported that TTF-1 is specifically expressed in pituicytoma, granular cell tumors, and SCO, and it is useful for distinguishing them from other sellar tumors.^[20] Those markers (S-100, GFAP, TTF-1, and galectin-3) seem to have limitations to differentiate SCO and pituicytoma.

In all 15 reported cases of SCO, the immunostain by EMA was available and showed positivity in every case. The immunostain by EMA was available in 32 cases of pituicytoma. EMA was negative in 28 (87.5%) cases and only focally positive in 4 cases. Therefore, EMA is considered to be important to distinguish these tumors.

There is little evidence for the sensitivity of SCOs to radiotherapy. Four of five SCO cases which underwent radiation therapy recurred.^[3,7,18] There also are limited

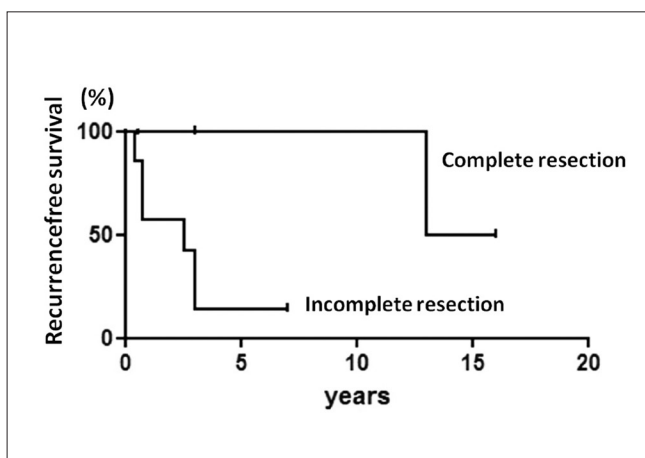


Figure 5: Recurrence-free survival curve of reported cases of spindle cell oncocytoma indicating an incomplete resection of the tumor was a significant risk factor for recurrence ($P = 0.0014$)

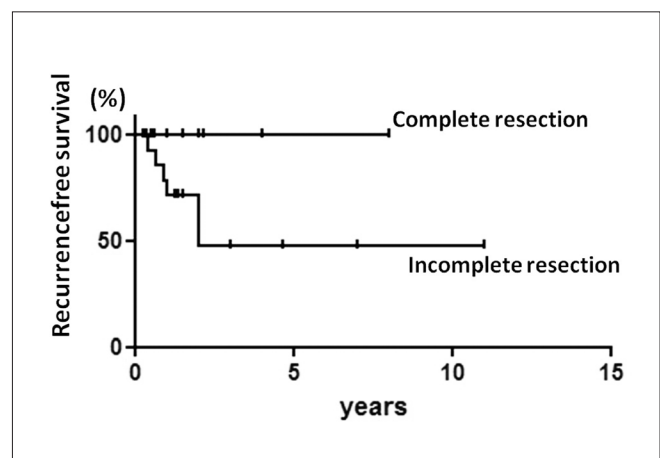


Figure 6: Recurrence-free survival curve of reported cases of pituicytoma indicating an incomplete resection of the tumor was a significant risk factor for recurrence ($P = 0.019$)

data on radiotherapy for pituitaryomas. Therefore, at the current time, no recommendations can be made regarding the effectiveness of adjuvant radiotherapy for these tumors. The effectiveness of stereotactic radiosurgery for these pathologies is not described previously. Based on our report and the literature, relative to other benign sellar lesions including meningioma, pituitary adenoma, and craniopharyngioma, radiosurgery appears to be a reasonable consideration for small-volume tumors not effacing or encasing the optic apparatus.

CONCLUSION

SCO of pituitary and pituitaryoma are rare entities with 15 and 45 cases reported to date, respectively, including our cases. Clinical behaviors of these tumors are very similar. Both tumors have a tendency to recur locally if not completely resected. The incomplete resection of the tumor was a significant risk factor for recurrence in both SCO and pituitaryoma ($P = 0.0014$ and $P = 0.019$, respectively). Both tumors have a tendency to be hypervascular, which may hamper total resection. EMA and mitochondria positivity is characteristic of SCO and they are considered to be important immunomarkers to distinguish these tumors.

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