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Spindle Cell Oncocytoma of the Anterior Pituitary Presenting with an Acute Clinical Course Due To Intraventricular Hemorrhage. A Case Report and Review of Literature

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: Male, 56
Final Diagnosis: Spindle cell oncocytoma of the adenohypophysis
Symptoms: Disturbed conscious level • visual disturbances
Medication: —
Clinical Procedure: Urgent craniotomy
Specialty: Neurosurgery

Objective: Rare disease
Background:

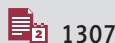
Spindle cell oncocytoma (SCO) is a rare nonfunctioning neoplasm of the adenohypophysis, and was first described in 2002. SCO has been categorized as a separate entity by the 2007 World Health Organization (WHO) and is classified as a Grade 1 tumor of the central nervous system (CNS). Review of the literature has shown that 33 cases of SCO have been reported to date, and most of them presented with a mass effect or with pan-hypopituitarism. However, all reported cases have described the tendency of SCO to be hypervascular on imaging and histology. We detail the first reported case of SCO to present with acute symptoms (pituitary apoplexy) and intraventricular hemorrhage, and review the literature on SCO.

Case Report: We report the case of 56-year-old man who presented suddenly with a severe headache and an altered level of consciousness. Brain magnetic resonance imaging (MRI) showed a suprasellar mass with hemorrhagic areas within the tumor and bleeding into the lateral ventricle with chiasmal and hypothalamic compression. The patient underwent urgent craniotomy, tumor resection and placement of an external ventricular drain (EVD). Histology and immunohistochemistry supported a diagnosis of SCO.

Conclusions: SCO of the adenohypophysis should be considered in patients who present suddenly with symptoms of pituitary apoplexy and intraventricular hemorrhage which may worsen the prognosis.

MeSH Keywords: Brain Neoplasms • Pituitary Apoplexy • Pituitary Neoplasms

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Background

Primary tumors of the anterior pituitary, or adenohypophysis, account for between 10% and 15% of all intracranial tumors. The spectrum of tumors at this site includes the most common, the pituitary adenoma, followed by craniopharyngioma, meningioma, oncocytoma, pituitary cytoma and granular cell tumor [1].

SCO of the adenohypophysis is a rare, benign, primary tumor in the sellar region, accounting for 0.1%–0.4% of all sellar tumors [2]. SCO was described as a new entity in 2002 by Roncaroli and colleagues and was classified as a distinct non-adenomatous sellar mass in the 2007 World Health Organization (WHO) classification [3,4].

Due to its rarity, little information is available regarding the imaging features and surgical characteristics of SCO. To our knowledge, there are only 34 cases reported to date (including our case). Most cases present with symptoms of slow onset that progress with as the tumor increases in size, resulting in compression of surrounding structures. Few cases presented with acute symptoms. Our case report is the first to describe a case presenting clinically with intratumoral bleeding and hemorrhage into the ventricles.

Case Report

A 56-year-old man presented to the emergency room (ER) with acute onset of a severe headache, vomiting, neck pain, back pain, and reduced level of consciousness. His son reported recently impaired visual acuity. On examination, the patient was stable and the Glasgow Coma Scale (GCS) score was 13/15 with no other neurological deficit. Following initial management in ER, the patient was sent for further investigations.

Magnetic resonance imaging (MRI) of the brain was performed using a 1.5 Tesla Siemens Avanto scanner. Multi-planar, multi-sequence images were obtained. Brain MRI showed a sellar and suprasellar macro-adenoma measuring 2.5×4.4×2.5 cm in its maximum anteroposterior, craniocaudal, and transverse dimensions, respectively, with intrasellar bleeding, and intraventricular hemorrhage extending into the fourth ventricle. Mild ventricular system dilatation was also noted, with chiasm and hypothalamic compression (Figures 1, 2).

The patient went for urgent sub-frontal craniotomy for tumor resection and placement of an external ventricular drain (EVD). Intra-operative tumor hypervascularity gave the macroscopic appearance of meningioma, and profuse bleeding limited the surgical resection. A sample of cerebrospinal fluid (CSF) was sent for analysis, and the tumor specimen was sent for histopathological examination and microbiological culture and sensitivity.

There were no significant abnormalities found on analysis of the CSF, Gram stain or culture and sensitivity. Light microscopy (Figure 3) with hematoxylin and eosin (H&E) staining showed interlacing fascicles of spindle cells, and epithelioid cells with eosinophilic cytoplasm containing numerous mitochondria (oncocytic change). The absence of cellular atypia, mitoses, invasion, and necrosis, together with a low cell proliferation rate on immunohistochemical staining with antibodies to Ki67 all supported the benign nature of the tumor. Immunohistochemical staining also showed that the tumor cells were uniformly positive for vimentin, S100, epithelial membrane antigen (EMA), and thyroid transcription factor-1 (TTF-1), and focally positive for glial fibrillary acidic protein (GFAP), and was negative for immunostaining with antibodies to CD34, smooth muscle actin (SMA), desmin, and pan-cytokeratin (CK).

Serological findings showed that the basal level of growth hormone (GH) was <0.10 ng/ml, morning cortisol level was 0.9 ug/dL, free triiodothyronine (T3) was 3.49 pmol/L, thyroid stimulating hormone (TSH) was 1.1819 uIU/mL, free thyroxine (T4) was 9.37 pmol/L, prolactin was 15.31 ng/mL, sodium (Na) was 131 mmol/L, and potassium (K) was 3.4 mmol/L.

The patient underwent good recovery with unchanged visual acuity but with a field defect in the left eye. He was referred for radiotherapy to control any residual tumor and showed no tumor recurrence at six-month follow-up.

Discussion

Spindle cell oncocytoma (SCO) is defined as an oncocytic, non-secreting, benign neoplasm of the adenohypophysis that presents in adults, with a mean age at presentation of 56 years [3,4]. These tumors may be indistinguishable macroscopically from a non-functioning pituitary adenoma and follow a benign clinical course, corresponding to World Health Organization (WHO) Grade 1 tumors of the central nervous system (CNS) [4].

Due to its benign clinical course and slow progression, review of the literature has shown that SCO usually presents with visual impairment (20 cases), which was the most common presenting symptom. Panhypopituitarism was the next most common symptom (15 cases) followed by headache (14 cases). Less commonly, SCO presented with vomiting, epistaxis, fatigue, syncope, polyuria, weight loss, oligomenorrhea, and amenorrhea (Table 1).

Abrupt neurologic deterioration may result from several etiologies associated with brain tumors, resulting in increased intracranial pressure (ICP). These causes include intracranial hemorrhage, infarction, cerebral edema, hydrocephalus, tissue necrosis, pituitary hemorrhage, and seizures. Pituitary infarction



Figure 1. Non-contrast head computed tomograph (CT), sagittal view, showing an isodense, sellar and suprasellar mass with a hyperdense area representing hemorrhage (star) and intraventricular hemorrhage extending to the fourth ventricle (black arrow).

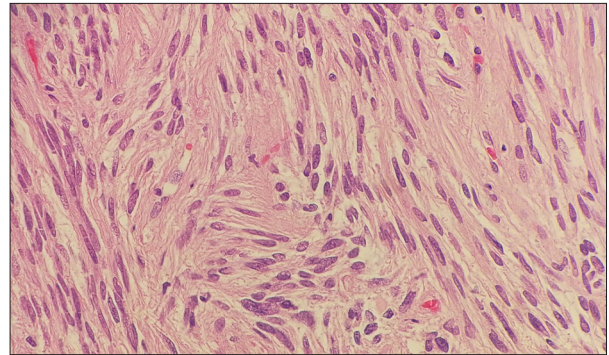


Figure 3. Photomicrograph of a hematoxylin and eosin (H&E) stained section of the tumor, showing interlacing fascicles of spindle cells and epithelioid cells, with no necrosis, mitoses, or invasion (x400).

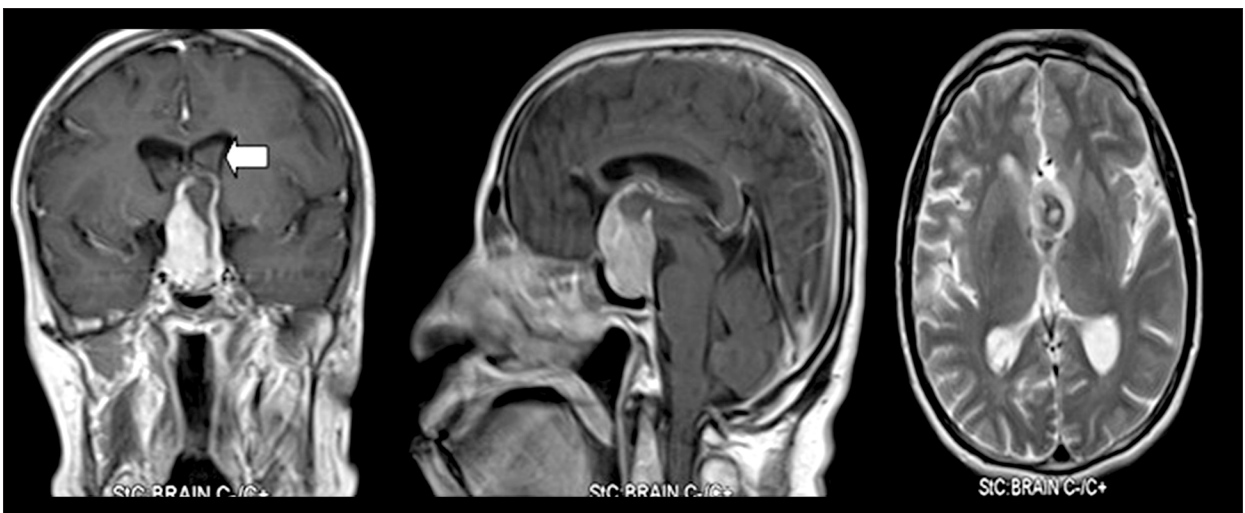


Figure 2. Magnetic resonance imaging (MRI) of the brain demonstrates a large sellar and suprasellar mass with an iso-intense signal with homogenous enhancement, apart from an area of acute intraventricular hemorrhage, which is also seen on the floor of the frontal horn of the lateral ventricle (white arrow) and down to the 4th ventricle.

and/or subsequent hemorrhage occur mainly from the compression effects of the tumor mass on the hypophyseal arteries against the edges of the sellar diaphragm. The signs and symptoms of pituitary hemorrhage (apoplexy) include abrupt onset of headache, ophthalmoplegia, visual disturbances, and changes in mental status [5].

Although the radiological findings have been reported to be non-specific in the literature, the characteristics of magnetic resonance imaging (MRI) and the different patterns of contrast enhancement may help to recognize this rare tumor. In

the recent publication from Hasiloglu and colleagues, they described the radiological findings of SCO, which include hypointense foci and linear signal-void areas on T1-weighted imaging and T2-weighted imaging [6]. On dynamic contrast-enhanced MRI (DCE-MRI) SCO shows intense contrast enhancement during the early stage of contrast administration (Hasiloglu's sign) [6]. The difficulty in distinguishing SCO from other tumors such as pituitary adenoma is important, because this tumor, unlike pituitary adenoma, tends to be very vascular and prone to hemorrhage during surgical resection [7]. This property of SCO is important to recognize, as hemorrhage can lead to the need

Table 1. Review of the literature on reported cases of spindle cell oncocytoma (SCO) of the anterior pituitary (adenohypophysis).

	Year	No.	Age/sex	Symptoms & signs	Imaging	Treatment	Histopathology	Recurrence
Roncaroli et al. [3]	2002	5	53–71 years 3 male 2 female	1/5 Pan-hypopituitarism 2/5 Visual field defects	5/5 Sellar mass with suprasellar extension	4/trans-sphenoidal 1/frontal craniotomy	Vimentin 5/5 EMA 5/5 S-100 4/5	No recurrence at 3 years
Dahiya et al. [14]	2005	2	1: 26/male 2: 55/female	1: Visual loss, panhypopituitarism 2: Headache, visual loss	1–2: Sellar/parasellar mass	1: Trans-sphenoidal, partial resection; difficult to dissect 2: Trans-sphenoidal, total resection; highly vascular mass	1–2: EMA S-100	1: Radiotherapy after initial surgery, no growth at 7 years 2: No recurrence at 6 months
Kloub et al. [15]	2005	2	1: 71/female 2: 76/male	1: Visual loss 2: Epistaxis	1: Sellar mass with suprasellar extension 2: Sellar mass with extension to nasopharynx	1: Trans-sphenoidal resection; firm fibrous tumor adherent to surrounding structures 2: Trans-sphenoidal resection; large necrotic tumor	1: Vimentin EMA S-100 Ki-67 18% 2: Vimentin EMA S-100 Ki-67 20%	1: Recurrence after 3 years from initial surgery, repeat surgery due to optic chiasm compression. 2: Recurrence after 3 years from initial surgery, received radiation therapy
Vajtai et al. [16]	2006	1	48/female	Visual loss	Sellar/parasellar mass with suprasellar extension	Trans-sphenoidal, total resection	Vimentin EMA S-100	No recurrence at 15 years
Farooq et al. [17]	2008	1	Male/76	Headache/weakness	Sellar/suprasellar	Trans-sphenoidal	S-100 and EMA	Radiotherapy after surgery, no growth at 2 years
Borota et al. [18]	2009	1	55/female	Headache, hypopituitarism	Sellar/suprasellar mass	Trans-sphenoidal, partial resection due to vascularity/bleeding	Vimentin EMA S-100 Ki-67 2%	Growth at 1 year, received radiotherapy, further growth after 10 months, stable afterwards
Coire, et al. [19]	2009	1	63/female	Visual loss, headache, panhypopituitarism	Sellar/suprasellar mass	Trans-sphenoidal, partial resection	Vimentin EMA S-100	Growth 5 months after initial surgery with optic chiasm compression. Repeat surgery followed radiotherapy

Table 1 continued. Review of the literature on reported cases of spindle cell oncocytoma (SCO) of the anterior pituitary (adenohypophysis).

	Year	No.	Age/sex	Symptoms & signs	Imaging	Treatment	Histopathology	Recurrence
Demssie et al. [20]	2009	1	59/ male	Visual loss, weight loss, vomiting, fatigue. Pan-hypopituitarism	Sellar/suprasellar mass	Trans-sphenoidal, partial resection; mass was noted to be firm and highly vascular	EMA S-100 Ki-67 1%	Growth at 9 months
Matyja et al. [2]	2010	2	1: 63/ female 2: 65/ female	1–2: Headache, visual loss, pan-hypopituitarism	1–2: Sellar/suprasellar mass	1: Trans-sphenoidal, total resection 2: Frontal approach, total resection	1–2: Vimentin EMA S-100	1: No recurrence at 28 months 2: Recurrence at 3 years, then repeat surgery with no recurrence 20 months after 2nd surgery
Borges et al. [21]	2010	1	70/ female	Visual loss	Sellar mass, heterogeneous features	Trans-sphenoidal resection, extensive bleeding	Vimentin S-100	Recurrence at 13 years
Mlika et al. [22]	2011	1	45/ female	Visual loss, headache	Sellar/suprasellar mass	Total resection, Trans-sphenoidal	Vimentin EMA S-100	No recurrence at 3
Romero-Rojas et al. [23]	2011	1	42/ female	Oligomenorrhea	Sellar mass	Resection	Vimentin EMA S-100	No follow-up mentioned
Ogiwara et al. [13]	2011	1	39/ male	Headache, visual loss, Pan-hypopituitarism, polyuria	Sellar/suprasellar mass	Trans-sphenoidal, partial resection due to firm and hypervascular mass	S-100 EMA TTF-1	1: Followed by radiotherapy with recurrence at 4 months then total resection-no recurrence at 1 year
Fujisawa et al. [24]	2012	1	68/ male	Visual loss, Pan-hypopituitarism	Sellar/suprasellar mass	Trans-sphenoidal, partial resection due to hypervascular and elastic mass	EMA S-100	Growth at 1.5 years followed by radiotherapy
Alexandrescue et al. [12]	2012	1	24/ female	headache, amenorrhea for 18 months, and new onset of left superior visual field disturbance of the left eye	Sellar/suprasellar	Sub-labial trans-septal approach	S100 EMA vimentin	No growth at 6 months

Table 1 continued. Review of the literature on reported cases of spindle cell oncocytoma (SCO) of the anterior pituitary (adenohypophysis).

	Year	No.	Age/sex	Symptoms & signs	Imaging	Treatment	Histopathology	Recurrence
Singh et al. [25]	2012	1	68/ male	Visual loss, headache	Sellar/suprasellar mass	Trans-sphenoidal, partial resection due to firm and hypervascular mass	Vimentin EMA	No growth at 5 months
Rotman et al. [26]	2014	1	80/ male	Visual loss, hypopituitarism, syncope	Sellar/suprasellar mass	Trans-sphenoidal, total resection	Vimentin EMA	Total resection/minimal growth at 8 years
Zygourakis et al. [27]	2015	2	1: 31/ female 2: 53/ female	1: Headache, visual loss 2: Headache	1: Sellar/suprasellar mass 2: Sellar/suprasellar mass	1: Trans-sphenoidal, partial resection 2: Biopsy, 7-mm lesion	1: Anti-mitochondrial Ab EMA 2: Anti-mitochondrial Ab EMA S-100	1: No recurrence at 6 months 2: No progression in 2 months
Mu et al. [28]	2015	2	1: 35/ female 2: 62/ female	1: Visual deficit, amenorrhea, galactorrhea 2: n/a	1: Sellar/suprasellar mass 2: Sellar/suprasellar mass	Total resection, craniotomy	1–2: Vimentin EMA S-100 TTF-1	1–2: No recurrence over 15–21 months
Custodio et al. [29]	2015	1	60/ male	Severe hyponatremia, pan hypopituitarism, visual deficit	Sellar/suprasellar mass	Trans-sphenoidal, partial resection, vascular mass	EMA S-100 Vimentin TTF-1	No growth at 18 months
Won Hyung et al. [30]	2015	1	49/ male	18-month history of malaise, decreased libido and hot flashes	Sellar/suprasellar	Trans-nasal trans-sphenoidal	vimentin, S100 TTF-1 EMA	
Mansour Mathkour et al. [31]	2015	1	59/ male	Headache	Sellar	Sub-labial trans-septal trans-sphenoidal	Vimentin, annexin, galectin, and S-100.	No growth at 4 years
Huy Gia Vuong et al. [32]	2016	1	70/ male	headache and visual Disturbane for 6 months.	Suprasellar-sellar	Tran-sphenoidal approach	Vimentin, TTF-1EMA and galectin-3. S-100	

to stabilize the patient, abort or defer surgery, or to consider embolization of the tumor vasculature [8].

Conservative treatment of pituitary hemorrhage (apoplexy) is rarely associated with reversal of hypopituitarism and may worsen the condition [9]. Open trans sphenoidal decompression of the hemorrhagic pituitary adenoma is the favored treatment for pituitary hemorrhage [10]. Unlike the trans-frontal approach, no brain retraction is needed, and trans-sphenoidal decompression is better tolerated by severely ill patients. A

craniotomy is reserved for patients with a non-aerated sphenoid sinus, a small sella with a large suprasellar mass, a narrow sellar diaphragm. with a dumb-bell shaped mass, or an associated intracerebral hematoma [11].

Alexandersecu and colleagues have proposed an explanation of why a minority of these tumors present with recurrence after an initial complete resection [12]. The expression of precursor neuronal immunomarkers, such as cytoplasmic pan-neuronal marker, SMI-311, expressed by the spindle cell

component, nestin and CD44 expressed by the epithelioid or polygonal cells of the tumor, may indicate that SCO of the adenohypophysis has a neuronal origin [12].

There is little evidence in the literature for the sensitivity of SCO to radiotherapy. Four of five published cases of SCO that underwent radiation therapy recurred. Therefore, at this time, no recommendations can be made regarding the effectiveness of adjuvant radiotherapy for SCO, and the effectiveness of stereotactic radiosurgery for treatment of this tumor has not been described [13].

Conclusions

A case of spindle cell oncocytoma (SCO) of the anterior pituitary (adenohypophysis) is presented, which has the unusual feature of an acute presentation (pituitary apoplexy) due to the presence of the intraventricular hemorrhage associated

with a large sellar and suprasellar tumor mass. Previously reported cases of SCO have been associated with hypervascularity, and problematic bleeding has been previously reported during surgical resection. Being aware of the possible diagnosis of SCO of the anterior pituitary is of clinical importance.

A review of the literature has shown that there is some evidence to suggest that different imaging patterns from dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) may be an aid to distinguishing SCO from other tumors of the adenohypophysis. However, SCO should be considered if peri-tumoral or intraventricular bleeding is present on initial imaging. In such cases, urgent surgery is indicated that should also include management of the effects of intraventricular hemorrhage.

Conflict of interest

None.

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