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(CASE REPORT)

Recurrent spindle cell Oncocytic pituicytoma. Case report of a rare tumor and a brief review of the literature

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Abstract

Spindle cell oncocytic pituicytoma (SCOP) is a rare, frequently misdiagnosed low-grade glial pituitary tumor of the posterior pituitary pituicytes. It is one of the sellar and suprasellar tumors, which also include pituitary adenomas, meningiomas, and granular cell tumors. Due to the imaging and histopathologic similarity of SCOPS to this set of sellar and suprasellar tumors, its diagnosis can be challenging, and frequently misdiagnosed as one of the other tumors. To differentiate SCOP from other tumors, immunohistochemistry (IHC) studies are essential. SCPOs belong to the family of Grade 1 tumors of the World Health Organization (WHO) classification of tumors. SCOPs are very vascular and adherent tumors, which cause difficulty in most cases during excision, leading to subtotal excision.

In this report, a multidisciplinary approach to the management of these tumors is emphasized, with the use of surgery as the main intervention along with adjuvant treatment and the use of longitudinal imaging. Occasional postoperative medical endocrine issues, including the development of a hypopituitarism phenomenon, will need close monitoring and hormonal treatment. It should be noted that recurrence is frequent despite the apparent control of the disease.

Greater awareness among the clinical community, and in particular, neurosurgeons, neuropathologists, and endocrinologists of SCOPS is essential for optimal diagnosis and management. Early diagnosis and correct identification are significant, not only to plan the surgical intervention, but also to differentiate the long-term plans of care and prevent underdiagnosis or a late spectrum of care.

The case complements the limited literature on this entity and is based on the need to always exercise vigilance, even with histologically benign tumors.

Keywords: Oncocytic pituicytoma; Spindle cell; Pituitary; Suprasellar tumors; Endoscopic transsphenoidal surgery; Benign

1. Introduction

The pituitary gland is a master endocrine gland located in the sellar region, a complicated anatomical region at the bottom of the brain. Although many types of lesions may occur in this site, the most frequent are pituitary adenomas. [1] Nevertheless, a wide range of non-adenomatous tumors, although not common, also pose a great challenge in

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diagnosis and treatment. Of these, spindle cell oncocytic pituicytoma (SCOP) is the rarest of all, and it is a unique diagnostic dilemma in the context of sellar and parasellar masses. [2]

SCOP is a benign, non-neuroendocrine, uncommon tumor of the posterior pituitary or infundibulum, which is considered to have a pituicytic origin, composed of specialized glial cells of the neurohypophysis. [3] It is also rare, as there are few cases reported in the world literature since its first description. This rarity is a frequent cause of diagnostic confusion, because its radiological and clinical appearance may resemble that of more prevalent sellar lesions, especially pituitary adenomas or meningiomas. [4] The absence of specific imaging features often makes a definitive diagnosis by histopathology necessary, and usually following surgical intervention. [5]

Clinical manifestations of patients with SCOP usually include mass effect manifestations, including visual field defects caused by optic chiasm compression, headache, and, less frequently, hypopituitarism in the case of severe impairment of the anterior pituitary gland. [4] These symptoms can also delay a correct diagnosis due to their insidious and nonspecific nature.

The main mode of treatment of SCOP is through surgical resection via the endoscopic transsphenoidal surgery (ETS) procedure. [6] SCOPs are highly vascular, however, and the tumor typically involves vital neurovascular structures (including the carotid arteries and the optic nerves) closely, making it potentially extremely difficult to surgically remove completely. [7] [9]

Gross total resection is not easily achieved, which predisposes to recurrence as the current case shows. Adjuvant radiation can be used in case of subtotal resection or recurrence to manage the growth of residual tumor or to avoid additional recurrence. (Iglesias P.2025) SCOP prognosis is overall good with complete resection due to its benign nature, with a long-term prognosis. Recurrence, however, is a possibility, particularly in cases of incomplete excision, and this is the reason why postoperative observation is of great significance. [1] [2] The purpose of the case report is to add to the knowledge of the rare tumor and describe a case of recurrent SCOP to give an idea about its clinical presentation, diagnostic peculiarities, and treatment difficulties, briefly reviewing the current literature to increase awareness and inform clinical practice in the future.

2. Case presentation

A 52-year-old female came to the clinic with a complaint of progressive headaches, dizziness, and blurring of vision over seven months. The symptoms were not serious at first, but they progressively worsened. She also reported that she had developed visual problems, which included blurred and double vision, eventually increasing and gradually causing limitation in her daily routine activities. The reported headache was predominantly frontal-based and at other times, retro-orbital. Occasionally, the headache was acute enough to disturb sleep and normal functioning. Of note, the patient was very reluctant to use non-prescription pain relievers. The patient also reported dizziness and chronic fatigue. Her medical history included well-controlled type II diabetes mellitus, hypertension, and hypercholesterolemia. Four years ago, she had a cholecystectomy. There was no reported significant medical family history.

Her combination of symptoms raised the suspicion of a sellar or suprasellar area lesion. In brain magnetic resonance imaging (MRI), a 2.2 cm mass was found in the Sella turcica with an extension to the suprasellar region. The MRI showed that the lesion was isointense on T1-weighted images, yet hyperintense compared to white matter on the T2-weighted images. The computed tomography (CT) scan showed a hyperdense mass to a minor degree. The imaging differential diagnosis was broad and included pituitary adenoma, meningioma, and craniopharyngioma. It was recommended that definitive management be done based on a tissue diagnosis.

The case was discussed in a multidisciplinary tumor board, and various diagnostic and treatment plans were discussed. The imaging appearance of the lesion, the patient preference, and easier surgical access came to be determinants in the choice of ETS as the method of choice. Lack of contraindicating characteristics determined the ETS surgical excision.

The ETS resection was done. During surgery, the tumor was found to be heavily vascular and adherent to surrounding structures, making it hard to be completely removed. The result was a subtotal resection, which postoperative contrast-enhanced MRI confirmed. The patient recovered well after surgery, with very few manageable complications. Adjuvant radiotherapy was started because of the incomplete excision.

Histopathological examination of the resected tumor revealed a moderately cellular vascular neoplasm, with predominantly elongated bipolar spindle cells. The tumor cells were arranged in crossing fascicles, occasional whorls, and rare storiform patterns. The cytoplasm was abundant, dense, variably eosinophilic, and finely granular, features

usually seen in oncocytic tumors. The nuclei were spindle-shaped to elongated, with pale chromatin, and the nucleoli were inconspicuous. There was no necrosis, and there were few mitotic figures (1 mitosis/10 high-power fields). The tumor did not show any morphologic features of neuroendocrine differentiation. (Figure 1A, B, C, D)

Since the tumor's histomorphological features were similar to those of other tumors in the sellar and parasellar areas, IHC studies were necessary to make a clear diagnosis. The tumor cells were intensely positive for S100, GFAP, EMA, TTF-1, and vimentin. There was a low proliferation index with 4% nuclear staining with Ki-67. Pituitary hormone stains, cytokeratin, chromogranin A, and synaptophysin stains were negative, and this contributed towards ruling out a pituitary adenoma and a neuroendocrine tumor.

The final diagnosis was consistent with a non-functional spindle cell oncocytic pituicytoma, WHO Grade I, a rare low-grade tumor of the posterior pituitary pituicytes. The 2021 WHO classification of pituitary tumors defines pituicytomas as TTF-1-expressing neoplasms within the posterior pituitary tumors. The postoperative period for the patient was unremarkable, and the patient was following a standardized neuroradiological follow-up program with a series of MRIs.

Nine months later, the patient experienced a recurrence, which was resected via ETS followed by radiation. The patient responded well to the treatment and resumed regular activities. With time, the patient exhibited symptoms of hypopituitarism, which were treated by hormone replacement therapy. At the last visit, 28 months before being lost to follow-up, the patient was neurologically stable and symptom-free. There was no evidence of additional recurrence experienced in serial imaging studies.

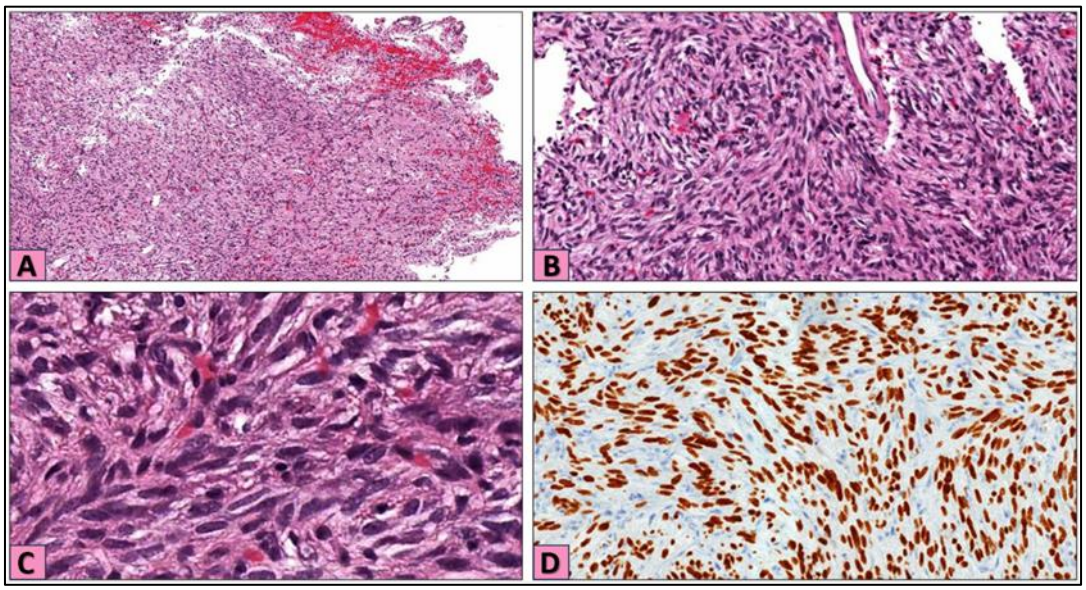

Figure 1 Histomorphology of spindle cell oncocytic pituicytoma (SCOP)

- **1A** Low power view showing a moderately cellular vascular neoplasm (H&E stain X20)
- **1B:** Intermediate power view showing the tumor cells arranged in crossing fascicles, whorls, and storiform patterns (H&E stain X40)
- **1C:** High power view showing the cytomorphologic details with abundant, dense, variably eosinophilic, and finely granular cytoplasm, features usually seen in oncocytic tumors. The nuclei are elongated, spindle-shaped, with pale chromatin, and the nucleoli are inconspicuous; no necrosis or mitotic figures (H&E stain X60)
- **1D**: Tumor cells positive for TTF-1

3. Discussion

3.1. History

Spindle cell oncocytic pituicytoma (SCOP) is a tumor that originates in the posterior lobe of the pituitary gland, specifically from pituicytes. It was not always recognized as a separate diagnostic entity. [**9**] In earlier literature, tumors with similar features were often labeled incorrectly, most commonly as nonfunctioning pituitary adenomas or granular

cell tumors. [10] The confusion stemmed largely from overlapping imaging features and nonspecific histologic appearances.

In the case presented here, the initial concern was for a sellar mass compressing the optic apparatus. Our working diagnosis was based on the patient's symptoms and the appearance of the lesion on imaging, and attention was focused on some more common masses in the sellar region. The definitive diagnosis was only made after resection, when histological evaluation provided greater clarity. The morphologic features alone raised suspicion for a rare glial neoplasm. Essential IHC analysis demonstrated strong nuclear staining for TTF-1, a finding that was key in establishing the diagnosis of SCOP. This pathologic pattern aligns with the small number of previously reported cases in the literature, all of which highlight the challenge of preoperative diagnosis. [4] [9]

3.2. Epidemiology

This tumor is rare. As of now, fewer than one hundred cases have been described in the literature. [5] Among those, the specific variant that shows both oncocytic change and spindle cell architecture is even less frequently documented. [10] It tends to occur in adults, usually in the fifth or sixth decade of life, which was true for our patient. No consistent trend in sex distribution has emerged from the available data. [2]

Because these tumors often resemble more common pituitary or parasellar lesions on imaging, they are likely underdiagnosed or misdiagnosed. [8] In centers without access to full immunohistochemical panels, confirmation may never be achieved. Retrospective reviews have shown that tumors once labeled as nonfunctioning adenomas or meningiomas were pituicytomas, identified only after recurrence or reoperation, prompting deeper pathologic analysis. [12]

3.3. Risk Factors

No environmental exposures, familial syndromes, or genetic mutations have been reported to be associated with spindle cell oncocytic pituicytoma. The tumor appears to occur sporadically. [5] This stands in contrast to other sellar region neoplasms, such as some pituitary adenomas, which may arise in the setting of inherited endocrine syndromes like multiple endocrine neoplasia. [4]

In the case of our patient, comorbidities included well-controlled type 2 diabetes, hypertension, and hyperlipidemia. These are common conditions and have no known relationship to this tumor type. At present, no predisposing factors have been identified in the literature. Its development appears to be random and unpredictable. [2]

3.4. WHO Classification

In 2022, the World Health Organization (WHO) revised its classification of the tumors located in the posterior pituitary gland. Earlier, it was classified into 4 distinct tumors in 2017 as pituicytoma, granular cell tumor (GCT), spindle cell oncocytoma (SCO), and sellar ependymoma. [3] Nonetheless, the above system was confusing as it failed to classify the tumors according to their shared cellular origin. To rectify this, the 2022 WHO classification re-classified them as subtypes of pituicytoma. This new system considers the fact that the four tumors (now known as traditional pituicytoma, oncocytic pituicytoma, granular pituicytoma and ependymal pituicytoma) have a common origin. This modification is indicative of a better understanding of the cellular origins. [3]

The tumors in this category are designated as grade 1. They are considered benign in terms of histology and proliferative index. However, they are often difficult to remove entirely. The tumor in our patient was highly vascular and adherent to surrounding structures, making complete excision technically unfeasible. This feature has been described in several prior reports and often results in subtotal resection followed by recurrence. [1]

Although these tumors are regarded low-grade, they may recur, more so when they cannot be completely removed. This scenario occurred with our patient. The tumor grew back in 9 months and necessitated a second operation and radiation therapy. This trend highlights the necessity to conduct imaging surveillance over the long term as well as a team approach to treatment planning.

3.5. Diagnosis

Given that the clinical presentation of SCOP is nonspecific, diagnosis typically requires evaluating multiple key features of the tumor that include its location, histopathologic features, and IHC studies. The diagnostic process typically begins with a baseline endocrine testing for an initial workup of sellar lesions, which is done to narrow the differential diagnosis

and rule out hormone-secreting pituitary adenoma as a possible diagnosis. [11] This is also done to assess the patient for possible hypopituitarism. This is also to evaluate the patient with regard to potential hypopituitarism.

A standard panel of pituitary hormones taken in the morning would consist of cortisol, thyroid-stimulating hormone (TSH), free thyroxin (T4), prolactin, insulin-like growth factor (IGF-1), luteinizing hormone (LH) and follicle-stimulating hormone (FSH). Serum pituitary hormones are generally normal in SCOP patients as seen in this patient and in most published cases, and this agrees with the fact that the tumor is a non-hormone secreting tumor. [8] [10] Normal hormone levels, along with the patient's clinical presentation, would prompt surgical removal and further assessment. Once tissue is retrieved during surgical resection, which can be complicated in some cases because of the tumor's location in the sellar region, adherence, and its hypervascularity, cytologic smears are immediately performed for a diagnosis as an intraoperative pathology consultation. [1]

The histologic and cytologic features of SCOP that are seen under the microscope include "fascicles of compact spindle cells with eosinophilic cytoplasm and occasional scattered pleomorphic cells". [12] The dense eosinophilic cytoplasm is a hallmark feature of the tumor, which is recognized to be a result of the abundance of mitochondria in the cell. This makes it have its characteristic "acidophilic granular cytoplasm" [12] SCOP is also noted to have a low mitotic activity and no mitosis, marking it as another key finding of the tumor, where case publications consistently report low Ki-67 proliferative index that range between 4-6%. [2] These unique characteristics, spindle cell configuration of the tumor, densely eosinophilic granular cytoplasm, and low Ki-67 proliferation index are what enable the pathologists to identify SCOP as was the case in the present case.

In addition to the characteristic histologic and cytologic appearance of the tumor, IHC is most often required to provide a clear and definitive diagnosis as seen in this patient. They are always positive on vimentin and S-100, markers related to pituicyte-derived neoplasms. [13] It also is usually positive to TTF-1 and epithelial membrane antigen (EMA) factors that assist in further narrowing the differential and support the fact that the tumor originated in a pituicyte lineage. [13] It is also noted that SCOP lacks immunoreactivity for pituitary hormones, cytokeratin, GFAP, and synaptophysin, which helps distinguish it from other neoplasms found in the sellar and suprasellar region. [4] This unique immunoprofile (TTF-1+, EMA+, S-100+, vimentin+, and pituitary hormone negative) is important in guiding pathologists toward a definitive diagnosis of SCOP, similarly to our case, where the tumor showed this same pattern, with intense TTF-1 and EMA positivity and negative staining for cytokeratin, synaptophysin, and pituitary hormones.

According to several published reports, molecular testing is not routinely required for diagnosis since no known molecular mutations have been identified in SCOP [1] Multiple reports have noted that BRAF mutations, which are typically seen in other CNS tumors, are not detected in SCOP, further supporting the idea that molecular analysis is not required. [1] [8]

3.6. Pathogenesis

SCOP, a low-grade neoplasm that originates in pituicytes, the specialized glial cells that supply the axons of the hypothalamic neurons in the posterior pituitary, is a rare, slow-growing neoplasm. SCOPs are silent infiltrators, the biology as mysterious as their clinical manifestation [5], in contrast to the hormone-secreting adenomas of the anterior pituitary.

The origin of SCOP is still unclear, but the most important evidence relates to the glial origin: SCOs are believed to originate from pituicytes, which are the modified astrocytes located in the neurohypophysis and infundibulum. [2] These cells usually support the vasopressin and oxytocin-secreting neurons structurally and metabolically. [2] SCOPs are immunohistochemically associated with TTF-1, a marker also expressed in pituicytes and certain tumors of the posterior pituitary. [13] This is an indication of a common developmental pathway, perhaps related to the embryologic origins of the ventral forebrain. Oncocytic change is the hallmark of the tumor, and the phenomenon of abnormal mitochondria accumulation in the cells can be observed and seen as eosinophilic granular cytoplasm. This could be a sign of metabolic change, but it is unclear what caused it.

3.7. Pathophysiology

SCOPs do not secrete hormones in contrast to functional adenomas. Rather, mass effect and compression have their influence on them. [4] The tumor presses upward against the optic chiasm as it enlarges, causing bitemporal hemianopia, the typical tunnel vision. [5] Dural distension and displacement of adjacent structures (e.g., diaphragma sellae) cause chronic, pressure-like headaches. [3] The anterior pituitary or the stalk may be compressed by large tumors, leading to partial deficiencies of hormones, but this is less frequent than in adenomas. [7] SCOPs are the

products of the posterior pituitary, and therefore, one would anticipate diabetes insipidus (DI), yet it is uncommon. This implies that the tumor does not affect the vasopressin axons, or it is compensating for the gradual injury.

3.8. Treatment and outcome

The management of SCOP, a rare WHO Grade I tumor of posterior pituitary origin, is challenging to manage due to its vascularity, adherence to surrounding structures, and its morphologic similarity to other sellar and suprasellar neoplasms. As with other posterior pituitary tumors, the primary approach to management is through the endoscopic transsphenoidal surgery (ETS) approach. [1] ETS is preferred due to its direct access, lower morbidity, and reduced risk of neurovascular injury when compared to transcranial methods. [9]

Complete resection can be difficult to perform, as these tumors are hypervascular and often infiltrative, particularly when the diagnosis is delayed. In this case, the intraoperative findings of vascularity and adherence limit the extent of resection, resulting in subtotal removal. [10] Residual tumor volume is an established indicator of recurrence, and therefore, adjuvant radiotherapy is recommended when the surgeon reports subtotal resection to improve local control. [11]

While there is no consensus on the timing or modality of radiotherapy due to the rarity of these tumors, fractionated stereotactic radiotherapy (FSRT) and intensity-modulated radiotherapy (IMRT) have demonstrated efficacy in controlling tumor progression in cases of residual or recurrent disease, as observed in our patient. [10] Some studies report radiologic stability in over 80% of patients receiving adjuvant therapy following subtotal resection. [6]

Prognosis is generally favorable, consistent with the tumor's low-grade classification and low mitotic index, with most patients experiencing long-term survival. However, recurrence is not uncommon, especially after incomplete resection, with time-to-recurrence ranging from 6 months to several years. [7] Our case demonstrates this pattern, with tumor recurrence occurring within 9 months, requiring repeat surgical excision followed by radiotherapy.

Endocrinologic complications, particularly hypopituitarism, are an important long-term consequence. They may result from tumor compression, surgical manipulation of the pituitary gland, or radiation-induced injury. [10] In our case, the patient developed hypopituitarism following recurrence and radiotherapy, requiring lifelong hormonal replacement therapy. Close longitudinal endocrinologic monitoring is therefore essential.

The typical surveillance includes serial MRI scans at 3 to 6 months during the first 2 years placed after surgery, and subsequent annual imaging in the case of a stable patient. It is of paramount importance to follow up with a multidisciplinary team comprising of neurosurgery, endocrinology, and neuro-oncology to identify any recurrence at an early stage and avoid complications of treatment. [9]

Overall, despite being histologically benign, SCOP is associated with a risk of recurrence and endocrine complications and is a surgical challenge necessitating a multidisciplinary, multimodal approach to management. Detection of the disease at an early stage and specific treatment plans are essential in enhancing patient outcomes and long-term quality of life. [10]

3.9. What lies ahead in the diagnosis and treatment of SCOP with the present technological revolution?

As we learn more about the rare neoplasms like the SCOP, there is an increased capacity of diagnosis and treatment of these neoplasms in a more specific manner. With the rapid development of molecular diagnostics and imaging technology, therefore, the future of SCOP management lies in integration, i.e., a combination of high-resolution neuroimaging, AI-aided diagnostic algorithms, and complete molecular profiling to result in improved detection of SCOP at an early stage and correct identification. Artificial intelligence (AI) is being trained to differentiate between complex sellar and parasellar tumors based on radiological patterns, which may soon be able to offer pre-invasive, algorithm-based initial diagnosis to eliminate any diagnostic delays. [14]

In the treatment aspect, the inability of conventional surgery and radiation to produce curative results in recurrent or adherent lesions like SCOP is opening the doors to precision medicine and targeted therapy. Possible molecular markers specific to tumors of pituicyte lineage, especially those involved in the MAPK/ERK or PI3K/AKT pathway, may provide a lead to future pharmacologic treatment. [15]

Also, the intraoperative technology, including real-time fluorescence-guided resection and intraoperative MRI, is improving the capability of making maximal safe resection and minimal collateral damage. [16] IHC and next-generation sequencing might soon be necessary not only in the diagnosis confirmation, but also in the assessment of the risk of

recurrence and response to therapy. [17] With the ongoing technological convergence with clinical practice, SCOP can become a more manageable tumor in the neuro-oncology panorama.

3.10. What did we Learn from this case?

The case presented an essential clinical and pathological lesson of diligence and the necessity of multidisciplinary cooperation when treating unusual sellar tumors. The onset of the case started with typical symptoms such as headache, dizziness, and visual disturbances, which did not indicate SCOP diagnosis at once, and the tumor had a nonspecific clinical and radiological picture. It also highlighted that a wide differential diagnosis should be maintained when dealing with sellar lesions particularly in case of uncharacteristic presentations and recurrence.

We also found out that despite highly skilled surgical management, gross total resection may be difficult due to the anatomical difficult location and tumor adherence, the necessity of adjuvant therapies and follow-up. Histopathology and IHC were also critical, not only to exclude the more frequent lesions such as pituitary adenomas or meningiomas, but also in establishing the pituicyte origin of this tumor. The recurrence, although unlucky, showed the lax but tenacious character of this WHO Grade I tumor which points out that benign histology does not always imply benign behavior.

In addition, the development of hypopituitarism indicated the need to perform an endocrine follow-up after surgery. In general, the case serves as another reminder that the successful management of rare tumors goes well beyond the operating room, into organized follow up, endocrine support, and patient education.

Abbreviations

- Spindle cell oncocytic pituicytoma (**SCOP**),
- Thyroid transcription factor-1 (**TTF-1**),
- Endoscopic transsphenoidal surgery (**ETS**),
- Immunohistochemical (**IHC**)

4. Conclusion

Spindle cell oncocytic pituicytoma (SCOP) is a rare and diagnostically difficult tumor of the sellar region, whose insidious clinical presentation and similar radiological characteristics require high index of suspicion and multidisciplinary approach to management. The case advocates the use of advanced imaging, histopathology, and immunohistochemistry to arrive at the right diagnosis. SCOP is a recurring disease, though a low-grade neoplasm, that can lead to long-term endocrine effects and close follow-ups and supportive care are critical. With the ongoing development of diagnostic modalities and specific treatment modalities, hopefully, in the future, there will be a greater capacity to treat this rare entity more effectively and individually.

Compliance with ethical standards

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Disclosure of conflict of interest

The following declarations are made by all authors:

- **Payment/services information:** All authors have declared that they received no financial support from any organization for the submitted work.
- **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might be interested in the submitted work.

Statement of ethical approval

Ethical review and approval were not required for this study involving human participants. The paper has been sufficiently anonymized to maintain the patient's confidentiality.

Statement of informed consent

The patient was lost to follow-up, and all attempts to reach the family members were unsuccessful. Therefore, the paper has been sufficiently anonymized to maintain patient confidentiality.

Data access statement

All relevant data are included in the paper.

Author contributions

All authors contributed equally to producing this manuscript.

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