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Review

When a Sellar Mass Is Not a Pituitary Adenoma: A Literature Review and Lessons from a Case of Pituicytoma

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Abstract

Background: Pituicytomas are rare, low-grade gliomas arising from pituicytes in the posterior pituitary or infundibulum. Due to its rarity and nonspecific clinical and radiological characteristics, it is frequently misdiagnosed as pituitary adenomas or other sellar tumors. Aims: To present an overview of pituicytoma, including clinical presentation, radiological and histopathological characteristics, differential diagnosis and treatment strategies, illustrated by a case report. Methods: A literature review was conducted to contextualize our patient with a sellar tumor, and to highlight key diagnostic and therapeutic considerations. Results/Case report: A 12-year-old boy presented with visual disturbances. MRI revealed a well-defined contrast-enhancing sellar mass, and the patient underwent transsphenoidal surgery. The diagnosis was assumed to be a nonfunctioning pituitary adenoma (NFPA). Two years later a residual tumor was treated with proton irradiation. Six years after the radiotherapy, the patient had epistaxis. Imaging showed a tumor in the sphenoidale sinus, which was surgically resected. The tumor had histopathological features of pituicytoma and immunoreactivity for TTF-1 and S100. The tissue from the first operation was reviewed, showing more characteristics with pituicytoma than NFPA, leading to redefinition of the initial diagnosis. Follow-up has been without any signs of residual tumor. Conclusions: Our case and literature review emphasize the importance of considering pituicytoma in the differential diagnosis among sellar lesions. The diagnosis relies on a combination of preoperative imaging, intraoperative findings and histopathology. Pituitary surgery is the first-line treatment, and the outcome is generally good. Increased awareness of pituicytomas is necessary to improve preoperative diagnostic accuracy and guide appropriate management.

Keywords: pituicytoma; pituitary insufficiency; sellar tumor; transsphenoidal surgery; histopathology; differential diagnoses

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1. Introduction

Posterior pituitary tumors (PPT) are rare, benign tumors originating from pituicytes. They include spindle cell oncocytomas, pituicytomas and granular cell tumors. This article focuses on pituicytomas, which represent approximately 0.07% of primary tumors in the sella and 50% of tumors in the posterior pituitary [1,2] and are classified as low-grade glial neoplasms (WHO grade I) [3,4].

Chu et al. reported in 2011 a total of 31 cases with a predominance of males [5]. Today more than 117 publications reporting one or more cases of pituicytoma are found when

combining the search for pituicytoma and case report in PubMed, and they seem to be equally frequent in men and women [1,2,6]. They are presented as case reports only or included in papers with, for example, a surgical [7] or a histopathological approach [8]. Pituicytomas occur most often in the middle decades of life (40–60 years) and are rare in children (3%) [1,2,6].

In the clinical setting, the patient with pituicytoma typically presents with a pituitary tumor on MRI, often discovered incidentally [2]. Pituicytoma can be intra- or more often suprasellar, but the radiological characteristics are nonspecific, and thus, it may be misclassified as pituitary adenoma. Symptoms of mass effect and endocrine dysfunction might be present [7,9]. Due to these uncharacteristic findings, the preoperative diagnosis of pituicytoma is usually difficult, and the diagnosis not obtained until the histopathological analysis is performed [10,11]. A total surgical resection is often difficult to obtain due to pituicytoma's high vascularization, the high risk of profuse bleeding during surgery, and the tumor's firm adhesion to adjacent structures. According to the literature, gross total resection varies between 50 and 60% [7], highlighting the need for improved preoperative identification. In addition, differential diagnosis of other tumors in the sella region is important. To highlight rare and clinically challenging presentations of pituicytoma, we conducted a targeted literature search in PubMed (pubmed.ncbi.nlm.nih.gov accessed on 10 Jun 2025).

The search focused on case reports and reviews describing pituicytomas in children, co-occurrence with hormone-producing pituitary adenomas, spontaneous tumor bleeding and other uncommon manifestations. The selected publications were reviewed by both authors, and based on this material, the present article provides an overview of pituicytoma and its differential diagnoses, including symptoms, diagnostics (macro- and microcharacteristics), treatment, as well as a patient case with an early presentation and unexpected course.

2. Tumors in the Hypothalamic–Pituitary Area: Pituicytomas and Differential Diagnoses

Tumors in the hypothalamic–pituitary area are usually benign, with pituitary adenomas being the most common and pituitary adenocarcinomas the rarest. Hormone-producing pituitary adenomas originate from the proliferation of the anterior pituitary hormone-producing cells [12]; in contrast, non-neuroendocrine sellar/suprasellar tumors are represented by a large and heterogeneous range of lesions with different origins. Included are various cysts, such as Rathke's cysts and pars intermedia cysts, craniopharyngiomas, meningiomas (arachnoid cells) or germinomas (primordial germ cell residuals). Other rarer tumors are schwannomas, gangliocytomas, neurocytomas, astrocytomas and pituicytomas. Pituicytomas account for approximately 0.07% of the cases [1,2,13–15].

Metastases from peripheral cancers, most commonly breast and lung cancer, may also be present [16]. In addition to tumors, inflammatory diseases such as hypophysitis as well as granulomatous diseases, for example, histiocytosis, tuberculosis and sarcoidosis, can also be seen. Aneurysm in the internal carotid artery might be present in this region as well, and all mentioned conditions can sometimes be difficult to distinguish from a tumor [14]. Thus, a broad range of differential diagnoses is essential to investigate as inflammatory and vascular lesions may also mimic neoplastic processes on imaging.

2.1. Pituicytoma

Pituicytoma is a tumor of the specialized modified glial cells of the posterior pituitary. These cells are known as "pituicytes", hence the name. This tumor has been classified in various ways, but in the 5th edition (2021) of the WHO classification of CNS tumors, pituicytomas are grouped together with granular cell tumors and spindle cell oncocytomas

of the pituitary gland, which are considered as variants of the same tumor, with the collective name posterior pituitary tumors. They all express thyroid transcription factor 1 (TTF1) [1,2], and the normal posterior pituitary also has several variants of pituicytes classified as oncocytic, granular and ependymal [15,17]. In older literature, pilocystic astrocytoma and pituicytoma are sometimes classified together since they are both derived from glial cells and they may share some characteristics such as GFAP positivity [4,18].

2.2. Differential Diagnoses

The diagnosis of pituicytoma is most often not established until the histopathological examination has been performed after surgery. When the pituicytoma is small and clearly localized to the infundibulum, the main differential diagnosis would be craniopharyngioma, hypophysitis or granulomatous disorders such as neurosarcoidosis and Langerhans cell histiocytosis, which all might present on MRI as a thickening of the pituitary stalk just like pituicytoma. When larger, it is more difficult to anticipate a pituicytoma as other lesions are far more common.

2.3. Symptoms of Tumors in the Hypothalamic–Pituitary Area

Smaller tumors in the hypothalamic–pituitary tract are mostly asymptomatic. When they become larger, they can cause hypopituitarism, visual impairment and, in rare cases, even hydrocephalus due to compression of the third ventricle.

Pituicytomas are usually discovered incidentally, i.e., incidentalomas, but they may also be found, for example, in the investigation of headaches and vertigo. The patient might also present with visual disturbance and/or symptoms caused by hypopituitarism (see, for example, ref. [6]). Additionally, hyperprolactinemia may occur due to compression of the pituitary stalk and thereby disturbance of the dopaminergic inhibition of prolactin secretion, which might secondarily cause oligomenorrhea, hypogonadism and galactorrhea. A systematic review that summarized all published clinical cases of posterior pituitary tumors found that out of 266 cases, 10 had Cushing and 5 acromegaly [6]. A recent review of the literature found that 20 cases out of 400 posterior pituitary tumors were reported following surgery for Cushing's disease [19].

Despite their location in the posterior lobe, these tumors are only rarely associated with diabetes insipidus, but this might be explained by the fact that the cell bodies of the vasopressin-secreting neurons remain intact in the hypothalamus [20].

2.4. Radiology

Pituicytomas typically appear as homogeneously contrast-enhancing lesions on CT, located within the sella or in the suprasellar region. Size is variable, ranging from a few millimeters to centimeters. They do not contain calcifications, which distinguishes them from craniopharyngiomas.

MRI usually shows a solid and contrast-enhancing mass due to its high vascularity, which can be isointense or hypointense on T1 weighted images and isointense to hyperintense on T2 weighted images. The bright spot in the posterior pituitary is often absent, and there are some radiological clues that can help to identify pituicytomas on MRI. Feng et al. suggest considering masses in the suprasellar region as pituicytomas when they are hypo- or isointense on T1 and hyperintense on T2 weighted MRI, with avid contrast enhancement on T1 weighted, and with no cyst component, calcification, infiltration of cavernous sinuses or cerebral edema. According to the authors, using these radiological features, the diagnosis of pituicytoma can be determined in over 90% of cases. The intratumorally flow voids (low-signal images representing fast-flowing blood within vessels) which are seen frequently in hypervascularized tumors are also indicative of pituicytoma [6,21].

Pituicytomas are also homogenous on PET and most often show a low to moderate uptake of FDG (fluorodeoxyglucose) [22].

Pituicytomas have a rich capillary network, accounting for their contrast enhancement and propensity to bleed at surgery. They receive their blood supply from the normal and extensive supply to the pituitary gland, including the meningo-hypophyseal trunk and superior hypophyseal arteries. Enlargement of the superior hypophyseal arteries is sometimes observed on angiography [23], and if performed preoperatively, it is valuable in decreasing the risk of intraoperative bleeding.

2.5. Histopathology

Histologically, pituicytomas are well-defined tumors composed of elongated eosinophilic bipolar spindle or stellate cells with rich vascular supply. The tumor cells have similarities to the normal neurohypophysis and are arranged in interlacing fascicles or dense storiform patterns [4,8]. Pituicytomas are immunoreactive for TTF-1; frequently positive for GFAP, S-100 protein, vimentin and cytokeratin AE1/AE3; occasionally positive for EMA; and negative for synaptophysin and chromogranin. The expression of GFAP, although often present, may vary due to the tumor's origin from a different pituicyte and the degree of cellular differentiation. The proliferation index Ki67 is usually less than 2% [5,11,15,24].

The granular cell variant of the posterior pituitary tumors consists of polygonal cells with conspicuous granular eosinophilic cytoplasm. The ependymal variant forms ependymal-type rosettes. This variant has sometimes, but not in the WHO classification, been classified as a separate subtype of pituitary posterior tumor. On electron microscopy, the tumor cells are spindled or polygonal with well-formed desmosomes, intercellular junctions, and phagolysosomes with electron-dense membranous debris but no secretory granules. The granular cells variant tends to grow even more slowly compared to the pituicytomas, and it is often found as a small, clinically asymptomatic incidental finding, often at autopsy [15,24].

The oncocytic variant of the posterior pituitary tumors has abundant eosinophilic cytoplasm filled with markedly dilated mitochondria, giving the tumor its oncocytic appearance. These tumors are also slow-growing but with a proliferation rate, Ki67, usually less than 5% [15,24].

The immunohistochemical profiles of posterior pituitary tumors are similar but not identical (Table 1).

Table 1. Histopathological, immunohistochemical (+positive, −negative) and radiological characteristics of the differential diagnosis to pituicytomas.

Type of Sellar Mass	Histopathological Features	Immunohistochemical Features	Radiological Features
Pituicytoma	Elongated eosinophilic spindle or stellate cells, interlacing fascicles or storiform patterns. Shares a methylation profile with granular cell tumors and spindle cell oncocytomas.	TTF-1+, S-100+, Vimentin+, Cytokeratin AE1/AE3+, usually GFAP+, EMA−, SYN−, Chromogranin-	Well-defined, solid, enhancing mass
Granular Cell Tumor	Polygonal cells with granular eosinophilic cytoplasm. Shares a methylation profile with pituicytomas.	S-100+, CD68+, Vimentin+, GFAP−	Well-defined, solid, enhancing mass

Table 1. *Cont.*

Type of Sellar Mass	Histopathological Features	Immunohistochemical Features	Radiological Features
Spindle Cell Oncocytoma	Abundant eosinophilic cytoplasm with dilated mitochondria. Shares a methylation profile with pituicytomas.	TTF-1+, GFAP+, Vimentin+, Cytokeratin AE1/AE3+, EMA+, SYN−, Chromogranin−	Well-defined, solid, enhancing mass
Pituitary Adenoma	Monomorphic cells, often chromophobic, acidophilic or basophilic.	Hormone markers (e.g., prolactin, GH, ACTH), Cytokeratin+, EMA+, chromogranin+, synaptophysin+	Variable enhancement, often solid or cystic
Craniopharyngioma (adamantinomatous)	Stratified squamous epithelium with palisading basal cells, "wet keratin", calcifications, cystic areas.	Beta-catenin+, Cytokeratin+, EMA+, GFAP−	Mixed solid and cystic, calcifications
Cranopharyngioma (papillary)	Well-differentiated squamous epithelium without palisading, papillary structures, no wet keratin or calcifications.	BRAF V600E+, EMA+, Cytokeratin+, Beta-catenin−, GFAP−	Usually solid, may have small cysts
Meningioma	Whorls of spindle cells, psammoma bodies.	EMA+, Vimentin+, S-100+, Cytokeratin−	Dural tail sign, enhancing mass
Pituitary Metastasis	Varied, often resembling primary tumor histology.	Varied, depending on primary tumor	Variable, often enhancing mass
Sellar Schwannoma	Antoni A and B areas, Verocay bodies.	S-100+, GFAP+, EMA−	Enhancing mass, often with cystic components
Pilocytic Astrocytoma	Bipolar cells with Rosenthal fibers, Eosinophilic granular bodies.	GFAP+, BRAF V600E+	Cystic with enhancing mural nodule
Hypophysitis	Lymphocytic infiltration, fibrosis.	CD3+, CD20+, IgG4+	Enhancing mass, often with thickened pituitary stalk
Neurosarcoidosis	Non-caseating granulomas, multinucleated giant cells	ACE+, CD68+, S-100+	Enhancing mass, often with thickened pituitary stalk

No specific genetic mutation linked to the posterior pituitary tumors, including the pituicytoma, has been discovered so far [25].

3. Treatment

First-line treatment of pituicytoma is transsphenoidal pituitary surgery, with a total gross resection rate varying between 40% and 100% [26]. The tumors are solid and well-demarcated, in many cases hard and firm, attached to surrounding structures with a high vascularity and high risk of bleeding during surgery. Preoperative embolization might be necessary [10], and therefore, a complete tumor resection is often not possible [6]. Transsphenoidal surgery is the most common surgical approach for smaller tumors, whereas for larger suprasellar tumors and residual tumors, a craniotomy approach might be required. Adjuvant radiotherapy, including stereotactic gamma knife or proton therapy, is recommended to manage residual or recurrent tumors. The gamma knife has high precision for well-defined lesions but may be contraindicated, for example, in tumors adjacent to the optic chiasm or optic nerves. Proton therapy provides a favorable dose distribution and may be preferred in such cases due to its ability to spare surrounding critical structures. Other therapies are generally not used. However, pituicytomas are generally positive

for the vascular endothelial growth factor receptor (VEGFR), and most of them, but not all, express somatostatin receptor (SSTR) 3 and 5, indicating a possible treatment option through targeted therapies in cases where resection remains insufficient [27].

Intraoperative bleeding has been reported in up to 75% of patients with pituicytoma, and the risk seems to increase with repeated surgeries [11,27]. Other surgical complications are partial or complete hypopituitarism, transient or permanent diabetes insipidus, and vision deterioration [11,28,29].

Five-year survival is very good when resection is complete, but when it is subtotal, the recurrence rate is approximately 30–40% [8].

4. Case Presentation

A previously healthy 12-year-old boy presented with reduced vision. Ophthalmologic examination revealed bitemporal visual field defects. Upon further questioning, he reported occasional headaches, which had not significantly impacted his daily life. His growth chart and weight development had been normal. MRI revealed a sellar mass measuring 20 × 20 × 27 mm, without evidence of cystic components, necrosis or calcifications. The pituitary gland and stalk were not visible, and the optic chiasm was difficult to delineate but appeared to be displaced anteriorly and superiorly behind the mass. The anterior recesses of the third ventricle were obliterated, though no hydrocephalus was present. Using SIPAP classification, the tumor was graded as follows: Suprasellar 4, Parasellar 1, Infrasellar 0, Anterior 0, Posterior 0. The lesion was assessed as a nonfunctioning pituitary adenoma. Prolactin was slightly elevated, but the remainder of the pituitary axis appeared intact. Hydrocortisone was initiated prophylactically. The patient underwent transsphenoidal surgery within two weeks. Postoperatively, he developed panhypopituitarism, including diabetes insipidus. Hormone replacement therapy continued with hydrocortisone and levothyroxine (Levaxin), and treatment with desmopressin (Minirin) was initiated. Visual field defects were completely resolved postoperatively. Histopathology confirmed a nonfunctioning pituitary adenoma with a heterogeneous proliferation pattern, with Ki-67 reaching up to 6% in certain areas, prompting close MRI surveillance every 3 months initially. Postoperative MRI showed changes consistent with surgical intervention. However, a small residual tumor could not be excluded. As the patient remained stable, growth hormone therapy was initiated. Since he was prepubertal, testosterone therapy was deferred.

Two years later, MRI revealed a 4–5 mm contrast-enhancing lesion anterior to the optic chiasm. Due to its proximity to the optic chiasm, complete surgical resection, as well as gamma knife radiation, was deemed too risky and challenging. Instead, the lesion was treated with proton beam therapy (1.8 Gy × 25 fractions). The treatment was well tolerated. Testosterone therapy was initiated, and the patient progressed through puberty without complications. Eight years postoperatively (6 years post-radiation), MRI showed nonspecific tissue in the sphenoid sinus, interpreted as mucosal thickening. One year later, the patient experienced significant epistaxis, and MRI revealed growth of the sphenoid sinus lesion. Surgical resection was performed. Vision and visual fields remained intact, and postoperative MRI showed no residual or recurrent tumor. Body mass index (BMI) was normal. The tumor had histopathological features of pituicytoma and immunoreactivity for TTF-1 and S100 but not GFAP. Ki67 was 3.4%. When tissue from the first operation was reviewed, it was found to share more characteristics with a pituicytoma than an NFPA, leading to reassessment of the initial diagnosis.

5. Discussion

Pituicytomas are rare tumors in the posterior pituitary, and they are often misdiagnosed due to their nonspecific radiological and clinical features. Radiological diagnosis is

often challenging, and like other tumors in this area, pituicytomas can be asymptomatic or present with hypopituitarism or by causing mass effect. First-line treatment is pituitary surgery, but radical surgical resection can be difficult due to the tumor's often firm attachment to surrounding normal tissue and high vascularity. Diagnosis is usually obtained from the histopathological analysis. In general, the tumors are TTF-1 and S-100 positive, mostly positive for vimentin, whereas GFAP expression seems to vary. Our case illustrates the diagnostic and therapeutic challenges associated with this tumor type, including recurrence despite radiotherapy and an unusual presentation with epistaxis, likely related to the tumor's hypervascularity and location of the residual. Although epistaxis is not a typical symptom of pituicytoma, it highlights the tumor's rich vascular supply, which has been noted intraoperatively in several reports [2,8,11]. Intraoperative bleeding can complicate surgical resection, and preoperative awareness of this feature may influence surgical planning. We have not found any other case reports of pituicytoma and epistaxis, but there are case reports of pituicytomas with spontaneous hemorrhage. For example, there is one case of a man with sudden onset severe headache who was found to have a hemorrhagic suprasellar mass with hemorrhage into the third ventricle, which was revealed to be a pituicytoma [30]. Our case is also not typical since pituicytoma is rare in children. By 2013, only three pediatric cases of pituicytoma had been reported [31]. In 2014, Cambiaso et al. reported four and a case of pituicytoma together with Cushing's disease in a 7-year-old girl [32]. In 2018, a case of a recurrent pituicytoma was reported in a pediatric patient [33].

There are also reported cases of adult patients with Cushing's disease as well as acromegaly (GH-producing adenoma) coexisting with pituicytoma. Even a paracrine relation between pituitary adenomas and pituicytoma has been proposed. In 2023, Rubino et al. reported two granular cell tumors and six pituicytomas, all of them coexisting with pituitary adenomas, seven functioning (six ACTH-producing and one GH-producing) and one nonfunctioning [34,35]. A recent review of the literature found that 20 cases out of 400 posterior pituitary tumors were reported following surgery for Cushing's disease [19]. Other rare case presentations include cystic pituicytoma [36] and recently a case diagnosed during pregnancy [37].

Hypopituitarism is a common complication of both the tumor and its surgical treatment. Our patient did not have any pituitary insufficiency before surgery, but postoperatively he developed pituitary insufficiency including diabetes insipidus and required hormone replacement therapy. Among 115 reported cases of pituicytoma, 61% presented with hypopituitarism [10]. In the study by Kremenevski, 66.7% had preoperative hypogonadism, hypothyroidism and hypocortisolism, but despite being a posterior pituitary tumor, no patient had arginine vasopressin deficiency [7]. This is in accordance with the findings in a meta-analysis, where only one patient had preoperative arginine vasopressin deficiency [38]. In most cases preoperative hormone deficiencies persist after surgery.

Visual disturbances are another common complication and were the presenting symptom in our patient. This recovered completely after surgery. In the review of Salge-Arrieta et al., approximately 55% of the patients had visual field defects. More than 1/3 of these patients improved post-surgery [11].

Due to the tumor's proximity to the hypothalamus, both the tumor and the surgery carry a risk of developing hypothalamic dysfunction including obesity. This problem was for the first time addressed in the retrospective study of 19 patients with posterior pituitary tumors, where an increase in BMI from 27.56 $\pm$ 6.73 to 30.21 $\pm$ 8.19 kg/m^2 after surgery was seen [7]. However, other factors such as evaluation of hyperphagia and doses of glucocorticoids, thyroxin, sex hormones and growth hormone were not included [39]. Our patient, who might have been expected to be particularly vulnerable due to his young age,

had a normal growth chart and has a normal BMI. Notably, his recurrent tumor was also unusual in its location since it occurred inferior to the sella.

6. Conclusions

In summary, pituicytomas are rare, low-grade gliomas of the posterior pituitary that often present diagnostic challenges due to their nonspecific clinical and radiological features. Increased awareness of this entity is crucial for improving diagnostic accuracy and optimizing patient outcomes. Our case highlights the importance of including pituicytoma in the differential diagnosis of sellar masses, particularly when imaging, and clinical presentation deviate from typical pituitary adenoma. Histopathological confirmation remains essential, with TTF-1 immunopositivity serving as a key diagnostic marker. Despite their generally indolent nature, recurrence may occur, underscoring the need for long-term follow-up and individualized management through a multidisciplinary approach (including neuroradiologists, neurosurgeons, endocrinologists and, when relevant, neuro-ophthalmologists).

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